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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
17 March 2005 (17.03.2005)

PCT

(10) International Publication Number
WO 2005/023858 A1

(51) International Patent Classification⁷: **C07K 14/47**,
16/18, G01N 33/68, A61K 38/17, C12N 15/12

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(21) International Application Number:
PCT/EP2003/013980

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(22) International Filing Date:
10 December 2003 (10.12.2003)

(81) Designated States (*national*): AE, AG, AI, AM, AT, AU,
AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR,
CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU,
SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
03019642.2 5 September 2003 (05.09.2003) EP

(84) Designated States (*regional*): ARIPO patent (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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Published:

— with international search report

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*



WO 2005/023858 A1

(54) Title: PROTEIN COMPLEXES ASSOCIATED WITH APP-PROCESSING

(57) Abstract: The present invention relates to protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

PROTEIN COMPLEXES ASSOCIATED WITH APP-PROCESSING

1. FIELD OF THE INVENTION

The present invention relates to protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

2. BACKGROUND OF THE INVENTION

Alzheimer's disease is a chronic condition that affects millions of individuals worldwide. After onset of the disease sufferers require a high degree of supervision and care. As the proportion of aged individuals in the population increases, the number of sufferers of Alzheimer's disease is expected to expand dramatically. Current top drugs (e.g. Aricept®/donepezil) attempt to achieve a temporary improvement of cognitive functions by inhibiting acetylcholinesterase, which results in increased levels of the neurotransmitter acetylcholine in the brain. These therapies are not suitable for later stages of the disease, they do not treat the underlying disease pathology, and they do not halt disease progression. The growing need for an effective therapy, coupled with the absence of effective treatments, presents a significant opportunity for drug target development and drug discovery.

The brains of sufferers of Alzheimer's disease show a characteristic pathology of prominent neuropathologic lesions, such as the initially intracellular neurofibrillary tangles (NFTs), and the extracellular amyloid-rich senile plaques. These lesions are associated with massive loss of populations of CNS neurons and their progression accompanies the clinical dementia associated with AD. The major component of amyloid plaques is the amyloid beta peptide. Amyloid beta is the proteolytic product of a precursor protein, beta amyloid precursor protein (beta-APP or APP). APP is a type-I trans-membrane protein which is cleaved by several different membrane-associated proteases. The first cleavage of APP occurs extracellularly by one of two proteases, alpha-secretase or beta-secretase. Beta-secretase or BACE1 (beta-site APP-cleaving enzyme) is a type-I

transmembrane protein containing an aspartyl protease activity (described in detail below). Alpha secretase is a metalloprotease whose activity is most likely to be provided by one or a combination of the proteins ADAM10 and ADAM17. Following either the beta or alpha cleavage of APP, the final cleavage event occurs within the membrane and is carried out by a protein complex called gamma secretase. It is the combination of the beta and gamma secretase activities that results in the liberation of the Abeta peptides of 40 and 42 residues (there are also lower levels of other forms) from the APP and ultimately the formation of the amyloid plaques responsible for the pathology of Alzheimer's disease. It is believed that the Abeta-42 peptide is the most critical Abeta species, because it shows the most pronounced neurotoxicity, and can aggregate easily, thus forming a nucleus for the aggregation of other Abeta peptides, such as the Abeta-40 which is typically produced at higher levels than the other species.

Cellzome's proprietary proteomics technology (TAP/LC-MS/MS) is particularly successful in the elucidation of membrane protein complexes. These multiprotein complexes form the core of the APP processing pathway and are not amenable to other techniques. Known proteins with an important functional role in APP processing were analysed with Cellzome's technology to comprehensively chart the dynamic protein interactions that contribute to Abeta production. Selected novel targets are subsequently validated using cellular or biochemical assays. Moreover, purified multi-protein complexes (e.g. beta- or gamma-secretase) do represent defined functional molecular machines, which are used to evaluate the mechanism of known compounds and for the optimisation of leads.

Presenilins

Presenilins 1 and 2 (PS1 and PS2) are integral membrane proteins which are localised in the endoplasmic reticulum, the Golgi and also at the cell surface [1]. They are predominantly found as a heterodimers of the NTF and CTF endoproteolytic fragments. The protease that cleaves presenilins (the "presenilinase") is not known, it is likely that the process is autocatalytic, also the functional significance of PS (auto)proteolysis is unclear.

Presenilins are involved in the proteolytical processing of Amyloid precursor protein (APP) [2] and the Notch receptor [3, 4]. In addition, Presenilins are associated

with the cell-adhesion proteins alpha and beta-catenin, N-cadherin, and E-cadherin [5] [6] and other members of the armadillo family [7] [8] [9] [10].

APP processing by Presenilins is through their effects on gamma-secretase which cleaves APP, generating the C-terminus of the A-beta peptide. PS1 associates with the C83 and C99 processed C-terminal fragments of APP [11], Nicastrin [12] and Pen-2 [13]. Aph-1 [14] [13] is required in Presenilin processing. It is not clear whether Presenilins regulate gamma-secretase activity directly or whether they are protease enzymes themselves [15]. The gamma secretase activity could comprise a multimeric complex of these proteins [12] [16] but it is not known how the relationship between these proteins affects secretase activity.

Familial Alzheimer's disease (FAD) patients carry mutations in the presenilin proteins (PS1; PS2) or in APP. These mutations result in increased production of A-beta42 [17] which is the main component of cerebral plaques in FAD [18].

Understanding the composition of the gamma-secretase complex, the relationship between its component parts and its regulation are important in the design of drugs for use in Alzheimer's disease patients.

Nicastrin

Nicastrin is a type 1 trans-membrane glycoprotein with a conserved transmembrane domain and DYIGS motif [12] which is constitutively expressed in neural cell lines [19]. Biochemical studies have shown that Nicastrin binds to Presenilins 1 and 2, C-terminal derivatives of APP [12], membrane-tethered forms of Notch [20] and that it is a member of the gamma-secretase complex along with PS1 and PS2 [16]. Gamma secretase activity is involved in the cleavage of both Notch and APP. It has been shown that Nicastrin is required for the intra-membrane cleavage of Notch [21] and APP [22], it may also have a role in post-translational stabilisation of Presenilin [23].

Aph-1 [14] and Pen-2 [13] were cloned recently in a screen for presenilin enhancers ("pen") in *C. elegans* and shown to interact genetically with Aph-2 (Nicastrin). Defects in Aph-1 affect Notch signalling and Nicastrin localisation [14]. Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins. Francis et al. [13] cloned the putative human orthologues of these genes, Aph-1a, Aph-1b and Pen-2, and recently Lee et al. [24] also cloned the human Aph-1 cDNAs.

The exact components of the gamma-secretase complex are not known but these two novel proteins could be components of or accessory factors to the complex and may interact together directly with Presenilin or with a Presenilin/Nicastrin complex. Nicastrin is therefore a member of the active gamma-secretase complex and there is recent evidence that it is the fully glycosylated form of the protein which is important in this complex. [25-29]

Aph-1

Goutte et al. [14] cloned aph-1 from *C. elegans*. Aph-1 encodes a novel conserved membrane protein with seven hydrophobic regions which are predicted to be membrane spanning. It has a 40 amino acid hydrophilic tail. *C. elegans* aph1 mutants have a phenotype which is indicative of a defect in Notch signalling. In these mutants, Aph-2 (Nicastrin) localisation is altered from being at the cell surface to being in the cytoplasm, concentrated around the nucleus. In *C. elegans*, Aph-1 interacts genetically with Aph-2 (Nicastrin) and Sel-12 (one of the *C. elegans* Presenilin genes) [13].

There are Human, Mouse, *Drosophila* Aph-1 homologues which are potential orthologues. Recently, the human Aph-1 homologues, hAph-1a and hAph-1b have been cloned [13, 24]. Aph-1a, the hypothetical CGI-78 protein, and Sambiasin isolated at Cellzome are all products of the same gene. Francis et al [13] showed that Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins in cultured *Drosophila* cells.

Lee et al. [24] cloned two splice variants of Aph-1a called Aph-1aS and Aph-1aL and Aph-1b. They have shown that mammalian Aph-1aL associates with Nicastrin and PS1 NTF/CTF heterodimers and with PS2 and Nicastrin in cultured cells and that endogenous Aph1aL associates with Nicastrin and PS1 in rat brain. Inhibition of the expression of Aph1a reduces the expression of both PS1 and PS2 but not Nicastrin and results in the accumulation of gamma-secretase substrates and the reduction of Abeta. Aph1a was also shown to be required for Notch cleavage.

Aph-1 may have a role in the maturation and trafficking of Nicastrin but it is necessary for gamma-secretase function and may be a member of the gamma-secretase complex.

Pen-2

Francis et al. [13] isolated pen-1 and pen-2 as two presenilin enhancer genes in a genetic screen in *C. elegans*. Pen-1 is identical to Aph-1 [14]. Pen-2 has two transmembrane domains and is thought to be a polytopic integral membrane protein. This group cloned the human homologues of Aph-1 and Pen-2. In *C. elegans*, Aph-1 and Pen-2 interact genetically with Aph-2 (Nicastrin) but not with each other. Hop-1 and Sel-12 are the *C. elegans* presenilin genes. Aph-2 interacts with Hop-1 whereas Aph-1 and Pen-2 interact with Sel-12 [13].

Pen-2 associates with PS1, PS2 and Nicastrin in mammalian cells and Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins in cultured *Drosophila* cells [13].

Nicastrin maturation is affected by the levels of PS1 and Pen-2. Loss of PS1 or a reduction in expression of Nicastrin reduces Pen-2 protein levels and a reduction in expression of Pen-2 decreases levels of both PS1, PS2 proteins. In addition, reducing the expression of Pen-2 by RNAi reduces the level of the PS1 complex [30]. These data suggest that Pen-2 is either a component of or regulates the assembly of the PS1 complex and that the expression of these proteins is co-ordinately regulated.

BACE1 (beta-secretase)

Vassar et al. [31] cloned a transmembrane aspartic protease that had the characteristics of the postulated beta-secretase of APP. Three other groups also cloned BACE1 using different approaches. BACE1 knockout mice have a normal phenotype, suggesting that therapeutic inhibition of BACE1 for AD may be free of mechanism-based toxicity. BACE1 ^{-/-} mice who are also homozygous for an amyloid precursor protein transgene lack brain beta-amyloid and beta-secretase-cleaved APP C-terminal fragments. [32]. Brain and primary cortical cultures from BACE1 knockout mice showed no detectable beta-secretase activity, and primary cortical cultures from BACE knockout mice produced much less amyloid-beta from APP. This suggests that BACE1, rather than its paralogue BACE2, is the main beta-secretase for APP.

BACE1 is a protein of 501 amino acids containing a 21-aa signal peptide followed by a proprotein domain spanning aa 22 to 45. There are alternatively spliced forms, BACE-I-457 and BACE-I-476. The luminal domain of the mature protein is followed by one predicted transmembrane domain and a short cytosolic C-terminal tail of 24 aa. BACE1 is predicted to be a type 1 transmembrane protein with the active site on the

luminal side of the membrane, where beta-secretase cleaves APP and possible other yet unidentified substrates. BACE1 mRNA in rat brain is present at higher levels in neurons than in glia, supporting that neurons are the primary source of the extracellular A-beta deposited in plaques. Sequence and mass spectrometry analyses showed that asn153, asn172, asn223, and asn354 of the BACE1 ectodomain are N-glycosylation sites. In addition, the ectodomain contains 6 cys residues that form disulfide bridges between positions 216 and 420, 278 and 443, and 330 and 380. The C-terminal domain of BACE1 contains a dileucine motif (LL499/500) that can potentially regulate its trafficking and endocytosis, and an adjacent serine, which is a casein kinase 1 phosphorylation site (S498) [33]. The propeptide is predominantly cleaved from BACE1 by furin [34]. In cells expressing wt or Swedish mutant APP, transient overexpression of BACE1 decreased alpha-secretase cleavage and increased beta-secretase activity at the known beta-secretase positions, asp1 and glu11. Although BACE1 is clearly a key enzyme required for the processing of APP into Ab, other potential substrates and functions of BACE1 are unknown. Also, no BACE1 interacting proteins with regulatory or modulatory functions have been described. Proteins that activate BACE1 activity would form suitable intervention points for Alzheimer's disease therapy. In addition, proteins that inhibit BACE1, like substrates or pseudosubstrates, could also provide suitable means of intervention e.g. as proteins therapeutics.

APP

APP is the precursor of Abeta, a peptide which forms the principal component of Alzheimer disease (AD) senile plaques [35] Masters et al. purified the cerebral amyloid protein that forms the plaque core in AD and Down syndrome. Van Nostrand et al. [36] presented evidence that nexin-II, a protease inhibitor that is synthesized and secreted by extravascular cells, is identical to APP. Multhaup et al. [37] demonstrated that APP is involved in copper reduction. They postulated that copper-mediated toxicity may contribute to neurodegeneration in AD, possibly by increased production of hydroxyl radicals. Yan et al. [38] reported that the receptor for advanced glycation end products RAGE is a receptor for the a-beta peptide and that expression of this receptor increases in AD. Expression of RAGE is particularly increased in neurons close to deposits of amyloid beta peptide and to neurofibrillary tangles. Kaneko et al. [39] demonstrated that nanomolar concentrations of various synthetic beta amyloids specifically impaired

mitochondrial succinate dehydrogenase, and speculated that one of the primary targets of beta amyloids is the mitochondrial electron transport chain.

Several missense mutations in the APP gene have been identified that result in early-onset AD: the Swedish APP670/671 double mutation; 3 different mutations at codon 717: the London APP717 mutation, V717I, V717F, and V717G; and the Florida APP716 mutation (Reviewed by Bertram and Tanzi [40]). Most of these AD-related mutations involve amino acid changes near the beta- and gamma-secretase cleavage sites. Two other missense mutations in the APP gene are located within A-beta near the alpha-secretase cleavage site: the Flemish APP692 mutation, which is associated with cerebral hemorrhage due to congophilic amyloid angiopathy or with early-onset AD with onset age in the mid-forties; and the Dutch APP693 mutation. Almost all AD-linked mutations do elevate secretion of A-beta-42, however, APP693 does not. [41]

Cao and Sudhof [42] demonstrated that the cytoplasmic tail of APP forms a complex with the nuclear adaptor protein Fe65 and the histone acetyltransferase TIP60. This complex stimulates transcription via heterologous Gal4 or LexA DNA binding domains, suggesting that release of the cytoplasmic tail of APP by gamma-cleavage may function in gene expression. The complex could modify expression of genes that function in inflammation [43] or apoptosis [44].

Weggen et al. [45] reported that the nonsteroidal antiinflammatory drugs ibuprofen, indomethacin, and sulindac can decrease the levels of high amyloidogenic amyloid-beta-42 peptide produced from a variety of cultured cells by as much as 80%. This effect was not seen in all NSAIDs and seemed not to be mediated by inhibition of cyclooxygenase (Cox) activity. Weggen et al. (2001) also demonstrated that short-term administration of ibuprofen to mice that produce APP lowered their brain levels of amyloid-beta-42. In cultured cells, the decrease in amyloid-beta-42 secretion was accompanied by an increase in the amyloid-beta(1-38) isoform, indicating that NSAIDs subtly alter gamma-secretase activity without significantly perturbing other APP processing pathways or Notch cleavage.

Proteins and other factors that regulate APP processing, and especially those that influence levels of Abeta-42 versus other Abeta species, form important potential targets in AD therapy.

Calsenilin

In a yeast two-hybrid screen with the C-terminus of Presenilin 2, a neuronal EF-hand (calcium-binding) protein was identified and named "calsenilin" [46]. It interacted with both Presenilin 1 and Presenilin 2 in cells and regulated the levels of a proteolytic product of Presenilin 2. Calsenilin is identical to KCHIP3, a protein which was found in a yeast two-hybrid screen for proteins interacting with A-type potassium channels (Kv4.3) [47]. KCHIP3 i) increased the density of Kv4.2 currents indicating a stabilisation of the channels at the plasma membrane; ii) shifted the current to hyperpolarized potentials; iii) slowed down the kinetics of inactivation and increased the kinetics of recovery.

Calsenilin is also identical to the transcriptional repressor DREAM which acts constitutively to suppress prodynorphin expression in spinal cord neurons [48]. Knocking out DREAM results in sufficient dynorphin expression to produce a strong reduction in generalized pain behavior, highlighting the role that intracellular molecules play in modulating pain gating in the spinal cord. Hence proteins that modulate Calsenilin/DREAM activity are interesting targets in nociception.

Tau

Neurofibrillary tangles (NFT), intraneuronal tau protein deposits, are hallmarks of several neurodegenerative disorders such as Alzheimer's and Pick's disease, frontotemporal dementia, cortico-basal degeneration and progressive supranuclear palsy.

The seven tau isoforms are all products of a single gene. Alternative splicing gives rise to six mRNA species differentially expressed in the CNS, depending on stage of neuronal maturation and neuron type. Tau is found mainly in the axon whereas a related protein, MAP2, is mainly found in dendrites.

Tau and MAP2 are microtubule-associated proteins (MAPs) which coassemble with microtubules and colocalise with microtubules in cells. Tau is a nonstructured molecule with a microtubule binding site containing 3 or 4 characteristic amino acid repeat in its carboxyl-terminal half. Alonso et al. [49] noted that in the brains of AD patients the neuronal cytoskeleton is progressively disrupted and replaced by tangles of paired helical filaments (PHFs), and that PHFs are composed mainly of hyperphosphorylated forms of tau. They demonstrated that in solution normal tau associated with the hyperphosphorylated AD P-tau to form large tangles of filaments. They also demonstrated that dephosphorylation with alkaline phosphatase abolished the ability of

AD P-tau to aggregate in vitro. In a form of autosomal dominant inherited dementia known as FTDP17 or Pick disease, the tau gene carries missense mutations or mutations in the 5'- splice site of exon 10, which results in increased levels of tau isoforms with 4 microtubule-binding repeats. These mutations lead to tau molecules that show reduced affinity for microtubules or are more prone to self aggregation.

Proteins and other factors that influence the affinity of tau protein for microtubules, and moreover, influence the aggregation of tau, which is probably mediated by phosphorylation and dephosphorylation events, are important potential targets in AD therapy.

Fe65

Fe65 is a PTB domain- and WW domain-containing adaptor protein that is part of protein complexes at the plasma membrane as well as in the nucleus: It interacts with the Alzheimer's disease amyloid precursor protein (APP; [50]) and related proteins APLP1 and APLP2 [51]. Binding of Fe65 to the cytoplasmic tail of APP enhances production of amyloid-forming Abeta peptides [52], but the molecular mechanism of this amyloidogenic effect of Fe65 has not been elucidated. Furthermore, Fe65 stabilizes AICD (APP Intracellular Domain), the cytosolic product of APP cleavage by gamma-secretase, [53] and forms a nuclear protein complex with TIP60 [42]. Little is known about the functional consequences of Fe65-dependent transactivation. The important role of TIP60 in interleukin-1beta- and NF-KappaB-dependent transactivation [43] suggests, however, that the Fe65 complex might function in inflammation.

Fe65 has been shown to bind to the transcription factor CP2/LSF/LBP1 [54] and the low-density lipoprotein receptor-related protein [55], but the significance of these interactions is unknown. Finally, Fe65 has been observed to block cell cycle progression by downregulating thymidylate synthase expression via an unknown mechanism [56].

Understanding the composition of the Fe65 complex, the relationship between its component parts and its regulation might therefore be important in the design of drugs for use in Alzheimer's disease patients as well as for the treatment of various inflammatory conditions and cancer.

X11beta

X11beta/Mint-2 is a neuronal adaptor protein that is believed to be involved in signal transduction processes. It is also regarded as a putative vesicular trafficking

protein in the brain that can form a complex with the potential to couple synaptic vesicle exocytosis to neuronal cell adhesion [57].

X11beta interacts with the Alzheimer's disease amyloid precursor protein (APP) [50]. Acting synergistically with Munc18a [58], X11beta stabilises APP and inhibits production of proteolytic APP fragments including the A beta peptide that is deposited in the brains of Alzheimer's disease patients [59].

Via a mechanism that depends on its PDZ domain (yet has otherwise not been characterized), X11beta potently inhibits transactivation by an APP-Gal4/VP16 fusion protein [58]. Besides interacting with APP, X11beta binds to the C-terminus of presenilin1, although not as strongly as does X11alpha [58]. In addition, X11beta has been reported to interact with XB51 [60], but the functional significance of this interaction is unknown.

In Drosophila, dX11beta overexpression in eye imaginal disks causes disruption of compound eye morphology due to enhanced apoptosis of neuronal cells [61]. X11beta has been shown to bind to NF-KappaB-p65 through its PDZ domain. This interaction has been implicated in NF-KappaB-dependent Abeta42 production [62].

Elucidation of X11beta complex composition and regulation might therefore help develop novel ways of therapeutic intervention in Alzheimer's disease and inflammation.

3. SUMMARY OF THE INVENTION

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
 - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions;and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, second column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm

DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising the proteins selected from the proteins in table 1, third column or a homologue thereof, or a variant thereof or functionally active fragments or functionally active derivatives of said proteins, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, but 1 to the number of proteins listed in table 1, fifth column of said complex, or a homologue or a variant thereof, or a functionally active fragment or functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins of said fifth column under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:
Expressing a protein of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the protein, preferably a tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a

functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to No.14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No.1 (a) and at least one of said proteins, being selected from the second group of proteins according to No.1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid encoding at least one protein selected from the first group of proteins according to No.1 (a) and the nucleic acid encoding at least one protein selected from the second group of proteins according to No.1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, which binds the complex of any of No.1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and/or an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the group of proteins according to No. 13.

18. A kit comprising in one or more containers the complex of any of No. 1 - 8 and/or the proteins of No. 13, optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
21. Array in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the proteins according to No. 13.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
25. A method for screening for a molecule that binds to the complex of any one of No. 1 - 8 and/or any of the proteins of No. 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a

functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex are determined.
40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody of fragment of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity or, or protein components of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or any of the proteins listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.

3.1 DEFINITIONS

The term "activity" as used herein, refers to the function of a molecule in its broadest sense. It generally includes, but is not limited to, biological, biochemical, physical or chemical functions of the molecule. It includes for example the enzymatic activity, the ability to interact with other molecules and ability to activate, facilitate, stabilize, inhibit, suppress or destabilize the function of other molecules, stability, ability to localize to certain subcellular locations. Where applicable, said term also relates to the function of a protein complex in its broadest sense.

The term "agonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, increases the amount of, or prolongs the duration of, the activity of the complex. The stimulation may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Agonists may include proteins, nucleic acids, carbohydrates or any other organic or inorganic molecule or metals. Agonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred activators are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 25%, at least 50%, at least 100%, at least, 200%, at least 500% or at least 1000% at a concentration of the activator $1\mu\text{g ml}^{-1}$, $10\mu\text{g ml}^{-1}$, $100\mu\text{g ml}^{-1}$, $500\mu\text{g ml}^{-1}$, 1mg ml^{-1} , 10mg ml^{-1} or 100mg ml^{-1} . Any combination of the

above mentioned degrees of percentages and concentration may be used to define an agonist of the invention, with greater effect at lower concentrations being preferred.

The term "amount" as used herein and as applicable to the embodiment described relates to the amount of the particular protein or protein complex described, including the value of null, i.e. where no protein or protein complex described in that particular embodiment is present under the or any of the conditions which might be specified in that particular embodiment.

The term "animal" as used herein includes, but is not limited to mammals, preferably mammals such as cows, pigs, horses, mice, rats, cats, dogs, sheep, goats and most preferably humans. Other animals used in agriculture, such as chickens, ducks etc. are also included in the definition as used herein.

The term "animal" as used herein does not include humans if being used in the context of genetic alterations to the germline.

The term "antagonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, decreases the amount of, or the duration or level of activity of the complex. The effect may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Antagonists may include proteins, including antibodies, nucleic acids, carbohydrates or any other organic or inorganic molecule or metals. Antagonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred antagonists are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 20%, at least 30%, at least 40% at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95% or at least 99% at a concentration of the inhibitor of $1\mu\text{g ml}^{-1}$, $10\mu\text{g ml}^{-1}$, $100\mu\text{g ml}^{-1}$, $500\mu\text{g ml}^{-1}$, 1mg ml^{-1} , 10mg ml^{-1} or 100mg ml^{-1} .

Any combination of the above mentioned degrees of percentages and concentration may be used to define antagonist of the invention, with greater effect at lower concentrations being preferred.

The term "antibodies" as used herein, include include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library.

The term "binding" as used herein means a stable or transient association between two molecules, including electrostatic, hydrophobic, ionic and/or hydrogen-bond interaction under physiological conditions and/or conditions being used in diagnostic or prognostic method or process or procedure.

The term "carrier" as used herein refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

If not stated otherwise, the terms "complex" and "protein complex" are used interchangeably herein and refer to a complex of proteins that is able to perform one or more functions of the wild type protein complex. The protein complex may or may not include and/or be associated with other molecules such as nucleic acid, such as RNA or

DNA, or lipids or further cofactors or moieties selected from a metal ions, hormones, second messengers, phosphate, sugars.

A "complex" of the invention may also be part of or a unit of a larger physiological protein assembly.

The term "component of the APP processing pathway" as used herein refers to a protein and/or protein complex which is involved in mediating APP processing in a cell. Components of the APP processing pathway include the following protein complexes as provided herein and components thereof:

Presenilin 1 complex, Presenilin 2 complex, Nicastrin complex, Aph-1a complex, Aph-1b complex, Pen-2 complex, BACE1 D215N complex, APP complex, APP695SW complex, APP-C99 complex, Tau complex, X11beta complex, Fe65 complex and Calsenilin complex.

If not stated otherwise, the term "compound" as used herein are include but are not limited to peptides, nucleic acids, carbohydrates, natural product extract librariesorganic molecules, preferentially small organic molecules, anorganic molecules, including but not limited to chemicals, metals and organometallic molecules.

The terms "derivatives" or "analogs of component proteins" or "variants" as used herein include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions. It means a protein which is the outcome of a modification of the naturally occurring protein, by amino acid substitutions, deletions and additios, respectively, which derivatives still exhibit the biological function of the naturally occurring protein although not necessarily to the same degree. The biological function of such proteins can e.g. be examined by suitable available in vitro assays as provided in the invention.

The term "functionally active" as used herein refers to a polypeptide, namely a fragment or derivative, having structural, regulatory, or biochemical functions of the protein according to the embodiment of which this polypeptide, namely fragment or derivative is related to.

The term "fragment" as used herein refers to a polypeptide of at least 10, 20, 30, 40 or 50 amino acids of the component protein according to the embodiment. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids.

The term "gene" as used herein refers to a nucleic acid comprising an open reading frame encoding a polypeptide of, if not stated otherwise, the present invention, including both exon and optionally intron sequences.

The terms "homologue" or "homologous gene products" as used herein mean a protein in another species, preferably mammals, which performs the same biological function as the a protein component of the complex further described herein. Such homologues are also termed "orthologous gene products". The algorithm for the detection of orthologue gene pairs from humans and mammals or other species uses the whole genome of these organisms. First, pairwise best hits are retrieved, using a full Smith-Waterman alignment of predicted proteins. To further improve reliability, these pairs are clustered with pairwise best hits involving *Drosophila melanogaster* and *C. elegans* proteins. Such analysis is given, e.g., in Nature, 2001, 409:860-921. The homologues of the proteins according to the invention can either be isolated based on the sequence homology of the genes encoding the proteins provided herein to the genes of other species by cloning the respective gene applying conventional technology and expressing the protein from such gene, or by isolating proteins of the other species by isolating the analogous complex according to the methods provided herein or to other suitable methods commonly known in the art.

The term "host cells" or, were applicable, "cells" or "hosts" as used herein is intended to be understood in a broadest sense and include, but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

It is understood that this term not only refers to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation of environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

The term "nucleic acid" as used herein refers to polynucleotides such as deoxyribonucleic acid (DNA), and, where appropriate, ribonucleic acid (RNA). They may also be polynucleotides which include within them synthetic or modified nucleotides. A number of different types of modification to polynucleotides are known in the art. These include methylphosphonate and phosphorothioate backbones, addition of acridine or polylysine chains at the 3' and/or 5' ends of the molecule. For the purposes of the present invention, it is to be understood that the polynucleotides described herein may be modified by any method available in the art. Such modifications may be carried out in order to enhance the in vivo activity or lifespan of polynucleotides of the invention. Polynucleotides according to the invention may be produced recombinantly, synthetically, or by any means available to those of skill in the art. They may also be cloned by standard techniques. The polynucleotides are typically provided in isolated and/or purified form. As applicable to the embodiment being described, they include both single stranded and double-stranded polynucleotides.

The term "percent identity", as used herein, means the number of identical residues as defined by an optimal alignment using the Smith-Waterman algorithm divided by the length of the overlap multiplied by 100. The alignment is performed by the search program (Pearson, 1991, Genomics 11:635-650) with the constraint to align the maximum of both sequences.

The terms "polypeptides" and "proteins" are, where applicable, used interchangeably herein. They may be chemically modified, e.g. post-translationally modified. For example, they may be glycosylated or comprise modified amino acid residues. They may also be modified by the addition of a signal sequence to promote their secretion from a cell where the polypeptide does not naturally contain such a sequence. They may be tagged with a tag. They may be tagged with different labels which may assist in identification of the proteins in a protein complex. Polypeptides/proteins for use in the invention may be in a substantially isolated form. It will be understood that the polypeptid/protein may be mixed with carriers or diluents which will not interfere with the intended purpose of the polypeptide and still be regarded as substantially isolated. A polypeptide/protein for use in the invention may also be in a substantially purified form, in which case it will generally comprise the polypeptide in a preparation in which more than 50%, e.g. more than 80%, 90%, 95% or 99%, by weight of the polypeptide in the preparation is a polypeptide of the invention.

"Target for therapeutic drug" means that the respective protein (target) can bind the active ingredient of a pharmaceutical composition and thereby changes its biological activity in response to the drug binding.

The term "tag" as used herein is meant to be understood in its broadest sense and to include, but is not limited to any suitable enzymatic, fluorescent, or radioactive labels and suitable epitopes, including but not limited to HA-tag, Myc-tag, T7, His-tag, FLAG-tag, Calmodulin binding proteins, glutathione-S-transferase, strep-tag, KT3-epitope, EEF-epitopes, green-fluorescent protein and variants thereof.

The term "therapeutics" as used herein, includes, but is not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments); antibodies thereto; nucleic acids encoding the component protein, and analogs or derivatives thereof; component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The term "vector" as used herein means a nucleic acid molecule capable of transporting another nucleic acid sequence to which it has been linked. Preferred vectors are those capable of autonomous replication and/or expression of nucleic acids to which they linked. The terms "plasmid" and "vector" are used interchangeably herein when applicable to the embodiment. However, vectors other than plasmids are also included herein. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

4. DETAILED DESCRIPTION OF THE INVENTION

Overview:

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said protein complex were identified. The components are listed in table 1.

Said object is further achieved by the characterisation of component proteins. These proteins are listed in table 2.

The invention thus relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
 - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions;and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, second column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or

homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising the proteins selected from the proteins in table 1, third column or a homologue thereof, or a variant thereof or functionally active fragments or functionally active derivatives of said proteins, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, but 1 to the number of proteins listed in table 1, fifth column of said complex, or a homologue or a variant thereof, or a functionally active fragment or functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins of said fifth column under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM

EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:
Expressing a protein of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the protein, preferably a tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to No.14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No.1 (a) and at least one of said proteins, being selected from the second group of proteins according to No.1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid encoding at least one protein selected from the first group of proteins according to No.1 (a) and the nucleic acid encoding at least one protein selected from the second group of proteins according to No.1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and/or an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the group of proteins according to No. 13.
18. A kit comprising in one or more containers the complex of any of No. 1 - 8 and/or the proteins of No. 13, optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
21. Array in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the proteins according to No. 13.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
25. A method for screening for a molecule that binds to the complex of any one of No. 1 - 8 and/or any of the proteins of No. 13, comprising the following steps:

- (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said

amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex are determined.
40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or any of the proteins listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.

Animal models are also provided herein.

Preferably, the protein components of the complexes described herein are all mammalian proteins. The complexes can also consist only of the respective homologues from other mammals such as mouse, rat, pig, cow, dog, monkey, sheep or horse or other species such as *D. melanogaster*, *C. elegans* or chicken. In another preferred embodiment, the complexes are a mixture of proteins from two or more species.

TABLES:

Table 1: Composition of Complexes

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Entry point'): Lists the bait proteins that have been chosen for the purification of the given complex.

Third column ('All interactors'): Lists all novel interactors which have been identified as members of the complex and all interactors which have been known to be associated with the bait so far.

Fourth column ('Known interactors'): Lists all interactors which have been known to be associated with the bait so far.

Fifth column ('Novel interactors of the complex'): Lists all novel interactors of the complex which have been identified in the experiments provided herein.

Sixth column: Separately lists the members of the newly identified complex which have not been annotated previously.

Table 2: Individual Proteins of the Complexes

First column ('Protein'): Lists in alphabetical order all proteins which have been identified as interactors of the complexes presented herein.

Second column ('SEQ ID'): Lists the SEQ ID (Sequence Identifications) of the proteins herein as used herein.

Third column ('IPI-Numbers'): Lists the IPI-Numbers of the proteins herein. The IPI-Numbers refer to the International Protein Index created by the European Bioinformatics Institute (EMBL-EBI), Hinxton, UK.

Fourth column ('Molecular Weight'): Lists the Molecular Weight of the proteins in Dalton.

Table 3: Biochemical Activities of the Complexes of the invention.

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Biochemical Activity'): Lists biochemical activities of the complexes. Assays in order to test these activities are also provided herein (infra).

4.1 PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The protein complexes of the present invention and their component proteins are described in the Tables 1 - 3. The protein complexes and component proteins can be obtained by methods well known in the art for protein purification and recombinant protein expression. For example, the protein complexes of the present invention can be isolated using the TAP method described in Section 5, infra, and in WO 00/09716 and Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032, which are each incorporated by reference in their entirety. Additionally, the protein complexes can be isolated by immunoprecipitation of the component proteins and combining the immunoprecipitated proteins. The protein complexes can also be produced by recombinantly expressing the component proteins and combining the expressed proteins.

The nucleic and amino acid sequences of the component proteins of the protein complexes of the present invention are provided herein (SEQ ID NO 1 - 266), and can be

obtained by any method known in the art, e.g., by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of each sequence, and/or by cloning from a cDNA or genomic library using an oligonucleotide specific for each nucleotide sequence.

Homologues (e.g., nucleic acids encoding component proteins from other species) or other related sequences (e.g., variants, paralogs) which are members of a native cellular protein complex can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular nucleic acid sequence as a probe, using methods well known in the art for nucleic acid hybridization and cloning.

Exemplary moderately stringent hybridization conditions are as follows: prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 µg/ml denatured salmon sperm DNA and 5-20 X 10⁶ cpm of ³²P-labeled probe. Washing of filters is done at 37°C for 1 hour in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 °C for 45 min before autoradiography. Alternatively, exemplary conditions of high stringency are as follows: e.g., hybridization to filter-bound DNA in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1xSSC/0.1% SDS at 68°C (Ausubel et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Other conditions of high stringency which may be used are well known in the art. Exemplary low stringency hybridization conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

For recombinant expression of one or more of the proteins, the nucleic acid containing all or a portion of the nucleotide sequence encoding the protein can be inserted into an appropriate expression vector, i.e., a vector that contains the necessary elements for the transcription and translation of the inserted protein coding sequence. The necessary transcriptional and translational signals can also be supplied by the native promoter of the component protein gene, and/or flanking regions.

A variety of host-vector systems may be utilized to express the protein coding sequence. These include but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

In a preferred embodiment, a complex of the present invention is obtained by expressing the entire coding sequences of the component proteins in the same cell, either under the control of the same promoter or separate promoters. In yet another embodiment, a derivative, fragment or homologue of a component protein is recombinantly expressed. Preferably the derivative, fragment or homologue of the protein forms a complex with the other components of the complex, and more preferably forms a complex that binds to an anti-complex antibody. Such an antibody is further described *infra*.

Any method available in the art can be used for the insertion of DNA fragments into a vector to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and protein coding sequences. These methods may include *in vitro* recombinant DNA and synthetic techniques and *in vivo* recombinant techniques (genetic recombination). Expression of nucleic acid sequences encoding a component protein, or a derivative, fragment or homologue thereof, may be regulated by a second nucleic acid sequence so that the gene or fragment thereof is expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins may be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the gene for the component protein. Promoters that may be used can be selected from among the many known in the art, and are chosen so as to be operative in the selected host cell.

In a specific embodiment, a vector is used that comprises a promoter operably linked to nucleic acid sequences encoding a component protein, or a fragment, derivative or homologue thereof, one or more origins of replication, and optionally, one or more selectable markers (e.g., an antibiotic resistance gene).

In another specific embodiment, an expression vector containing the coding sequence, or a portion thereof, of a component protein, either together or separately, is made by subcloning the gene sequences into the EcoRI restriction site of each of the three pGEX vectors (glutathione S-transferase expression vectors; Smith and Johnson, 1988, Gene 7:31-40). This allows for the expression of products in the correct reading frame.

Expression vectors containing the sequences of interest can be identified by three general approaches: (a) nucleic acid hybridization, (b) presence or absence of "marker" gene function, and (c) expression of the inserted sequences. In the first approach, coding sequences can be detected by nucleic acid hybridization to probes comprising sequences homologous and complementary to the inserted sequences. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "marker" functions (e.g., resistance to antibiotics, occlusion body formation in baculovirus, etc.) caused by insertion of the sequences of interest in the vector. For example, if a component protein gene, or portion thereof, is inserted within the marker gene sequence of the vector, recombinants containing the encoded protein or portion will be identified by the absence of the marker gene function (e.g., loss of β -galactosidase activity). In the third approach, recombinant expression vectors can be identified by assaying for the component protein expressed by the recombinant vector. Such assays can be based, for example, on the physical or functional properties of the interacting species in in vitro assay systems, e.g., formation of a complex comprising the protein or binding to an anti-complex antibody.

Once recombinant component protein molecules are identified and the complexes or individual proteins isolated, several methods known in the art can be used to propagate them. Using a suitable host system and growth conditions, recombinant expression vectors can be propagated and amplified in quantity. As previously described, the expression vectors or derivatives which can be used include, but are not limited to, human or animal viruses such as vaccinia virus or adenovirus; insect viruses such as baculovirus, yeast vectors; bacteriophage vectors such as lambda phage; and plasmid and cosmid vectors.

In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or modifies or processes the expressed proteins in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically-engineered component proteins may

be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation, etc.) of proteins. Appropriate cell lines or host systems can be chosen to ensure that the desired modification and processing of the foreign protein is achieved. For example, expression in a bacterial system can be used to produce an unglycosylated core protein, while expression in mammalian cells ensures "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

In other specific embodiments, a component protein or a fragment, homologue or derivative thereof, may be expressed as fusion or chimeric protein product comprising the protein, fragment, homologue, or derivative joined via a peptide bond to a heterologous protein sequence of a different protein. Such chimeric products can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acids to each other by methods known in the art, in the proper coding frame, and expressing the chimeric products in a suitable host by methods commonly known in the art. Alternatively, such a chimeric product can be made by protein synthetic techniques, e.g., by use of a peptide synthesizer. Chimeric genes comprising a portion of a component protein fused to any heterologous protein-encoding sequences may be constructed.

In particular, protein component derivatives can be made by altering their sequences by substitutions, additions or deletions that provide for functionally equivalent molecules. Due to the degeneracy of nucleotide coding sequences, other DNA sequences that encode substantially the same amino acid sequence as a component gene or cDNA can be used in the practice of the present invention. These include but are not limited to nucleotide sequences comprising all or portions of the component protein gene that are altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a silent change. Likewise, the derivatives of the invention include, but are not limited to, those containing, as a primary amino acid sequence, all or part of the amino acid sequence of a component protein, including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence resulting in a silent change. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity that acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the

sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

In a specific embodiment, up to 1%, 2%, 5%, 10%, 15% or 20% of the total number of amino acids in the wild type protein are substituted or deleted; or 1, 2, 3, 4, 5, or 6 or up to 10 or up to 20 amino acids are inserted, substituted or deleted relative to the wild type protein.

In a specific embodiment of the invention, the nucleic acids encoding a protein component and protein components consisting of or comprising a fragment of or consisting of at least 6 (continuous) amino acids of the protein are provided. In other embodiments, the fragment consists of at least 10, 20, 30, 40, or 50 amino acids of the component protein. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids. Derivatives or analogs of component proteins include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions.

In a specific embodiment, proteins are provided herein, which share an identical region of 20, 30, 40, 50 or 60 contiguous amino acids of the proteins listed in table 2.

The protein component derivatives and analogs of the invention can be produced by various methods known in the art. The manipulations which result in their production can occur at the gene or protein level. For example, the cloned gene sequences can be modified by any of numerous strategies known in the art (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The sequences can be cleaved at appropriate sites with restriction endonuclease(s), followed by further enzymatic modification if desired, isolated, and ligated in vitro. In the production of the gene encoding a derivative,

homologue or analog of a component protein, care should be taken to ensure that the modified gene retains the original translational reading frame, uninterrupted by translational stop signals, in the gene region where the desired activity is encoded.

Additionally, the encoding nucleic acid sequence can be mutated *in vitro* or *in vivo*, to create and/or destroy translation, initiation, and/or termination sequences, or to create variations in coding regions and/or form new restriction endonuclease sites or destroy pre-existing ones, to facilitate further *in vitro* modification. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis and *in vitro* site-directed mutagenesis (Hutchinson et al., 1978, *J. Biol. Chem.* 253:6551-6558), amplification with PCR primers containing a mutation, etc.

Once a recombinant cell expressing a component protein, or fragment or derivative thereof, is identified, the individual gene product or complex can be isolated and analyzed. This is achieved by assays based on the physical and/or functional properties of the protein or complex, including, but not limited to, radioactive labeling of the product followed by analysis by gel electrophoresis, immunoassay, cross-linking to marker-labeled product, etc.

The component proteins and complexes may be isolated and purified by standard methods known in the art (either from natural sources or recombinant host cells expressing the complexes or proteins), including but not restricted to column chromatography (e.g., ion exchange, affinity, gel exclusion, reversed-phase high pressure, fast protein liquid, etc.), differential centrifugation, differential solubility, or by any other standard technique used for the purification of proteins. Functional properties may be evaluated using any suitable assay known in the art.

Alternatively, once a component protein or its derivative, is identified, the amino acid sequence of the protein can be deduced from the nucleic acid sequence of the chimeric gene from which it was encoded. As a result, the protein or its derivative can be synthesized by standard chemical methods known in the art (e.g., Hunkapiller et al., 1984, *Nature* 310:105-111).

Manipulations of component protein sequences may be made at the protein level. Included within the scope of the invention is a complex in which the component proteins or derivatives and analogs that are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by

known techniques, including but not limited to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄, acetylation, formylation, oxidation, reduction, metabolic synthesis in the presence of tunicamycin, etc.

In specific embodiments, the amino acid sequences are modified to include a fluorescent label. In another specific embodiment, the protein sequences are modified to have a heterofunctional reagent; such heterofunctional reagents can be used to crosslink the members of the complex.

In addition, complexes of analogs and derivatives of component proteins can be chemically synthesized. For example, a peptide corresponding to a portion of a component protein, which comprises the desired domain or mediates the desired activity in vitro (e.g., complex formation) can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the protein sequence.

In cases where natural products are suspected of being mutant or are isolated from new species, the amino acid sequence of a component protein isolated from the natural source, as well as those expressed in vitro, or from synthesized expression vectors in vivo or in vitro, can be determined from analysis of the DNA sequence, or alternatively, by direct sequencing of the isolated protein. Such analysis can be performed by manual sequencing or through use of an automated amino acid sequenator.

The complexes can also be analyzed by hydrophilicity analysis (Hopp and Woods, 1981, Proc. Natl. Acad. Sci. USA 78:3824-3828). A hydrophilicity profile can be used to identify the hydrophobic and hydrophilic regions of the proteins, and help predict their orientation in designing substrates for experimental manipulation, such as in binding experiments, antibody synthesis, etc. Secondary structural analysis can also be done to identify regions of the component proteins, or their derivatives, that assume specific structures (Chou and Fasman, 1974, Biochemistry 13:222-23). Manipulation, translation, secondary structure prediction, hydrophilicity and hydrophobicity profile predictions, open reading frame prediction and plotting, and determination of sequence homologies, etc., can be accomplished using computer software programs available in the art.

Other methods of structural analysis including but not limited to X-ray crystallography (Engstrom, 1974, Biochem. Exp. Biol. 11:7-13), mass spectroscopy and gas chromatography (Methods in Protein Science, J. Wiley and Sons, New York, 1997), and computer modeling (Fletterick and Zoller, eds., 1986, Computer Graphics and

Molecular Modeling, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor Press, New York) can also be employed.

4.2 ANTIBODIES TO PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

According to the present invention, a protein complex of the present invention comprising a first protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in third column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, can be used as an immunogen to generate antibodies which immunospecifically bind such immunogen. According to the present invention, also a protein complex of the present invention can be used as an immunogen to generate antibodies which immunospecifically bind to such immunogen comprising all proteins listed in fifth column of table 1.

Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library. In a specific embodiment, antibodies to a complex comprising human protein components are produced. In another embodiment, a complex formed from a fragment of said first protein and a fragment of said second protein, which fragments contain the protein domain that interacts with the other member of the complex, are used as an immunogen for antibody production. In a preferred embodiment, the antibody specific for the complex in that the antibody does not bind the individual protein components of the complex.

Polyclonal antibodies can be prepared as described above by immunizing a suitable subject with a polypeptide of the invention as an immunogen. Preferred polyclonal antibody compositions are ones that have been selected for antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred polyclonal antibody preparations are ones that contain only antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression

of a polypeptide of the invention. In such a manner, the only human epitope or epitopes recognized by the resulting antibody compositions raised against this immunogen will be present as part of a polypeptide or polypeptides of the invention.

The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. If desired, the antibody molecules can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. Alternatively, antibodies specific for a protein or polypeptide of the invention can be selected for (e.g., partially purified) or purified by, e.g., affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, i.e., one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those on the desired protein or polypeptide of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein or polypeptide of the invention.

At an appropriate time after immunization, e.g., when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein, 1975, *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al., 1983, *Immunol. Today* 4:72), the EBV-hybridoma technique (Cole et al., 1985, *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally *Current Protocols in Immunology* 1994, Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the

hybridoma culture supernatants for antibodies that bind the polypeptide of interest, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a polypeptide of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al., 1991, *Bio/Technology* 9:1370-1372; Hay et al., 1992, *Hum. Antibod. Hybridomas* 3:81-85; Huse et al., 1989, *Science* 246:1275-1281; Griffiths et al., 1993, *EMBO J.* 12:725-734.

Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, e.g., Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Humanized antibodies are antibody molecules from non-human species having one or more complementarily determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, e.g., Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al., 1988, *Science* 240:1041-1043; Liu et al., 1987, *Proc. Natl. Acad.*

Sci. USA 84:3439-3443; Liu et al., 1987, J. Immunol. 139:3521-3526; Sun et al., 1987, Proc. Natl. Acad. Sci. USA 84:214-218; Nishimura et al., 1987, Canc. Res. 47:999-1005; Wood et al., 1985, Nature 314:446-449; and Shaw et al., 1988, J. Natl. Cancer Inst. 80:1553-1559); Morrison, 1985, Science 229:1202-1207; Oi et al., 1986, Bio/Techniques 4:214; U.S. Patent 5,225,539; Jones et al., 1986, Nature 321:552-525; Verhoeyan et al., 1988, Science 239:1534; and Beidler et al., 1988, J. Immunol. 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, 1995, Int. Rev. Immunol. 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., 1994, Bio/technology 12:899-903).

Antibody fragments that contain the idiotypes of the complex can be generated by techniques known in the art. For example, such fragments include, but are not limited to, the F(ab')₂ fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragment that can be generated by reducing the disulfide bridges of

the F(ab')₂ fragment; the Fab fragment that can be generated by treating the antibody molecular with papain and a reducing agent; and Fv fragments.

In the production of antibodies, screening for the desired antibody can be accomplished by techniques known in the art, e.g., ELISA (enzyme-linked immunosorbent assay). To select antibodies specific to a particular domain of the complex, or a derivative thereof, one may assay generated hybridomas for a product that binds to the fragment of the complex, or a derivative thereof, that contains such a domain. For selection of an antibody that specifically binds a complex of the present, or a derivative, or homologue thereof, but which does not specifically bind to the individual proteins of the complex, or a derivative, or homologue thereof, one can select on the basis of positive binding to the complex and a lack of binding to the individual protein components.

Antibodies specific to a domain of the complex, or a derivative, or homologue thereof, are also provided.

The foregoing antibodies can be used in methods known in the art relating to the localization and/or quantification of the complexes of the invention, e.g., for imaging these proteins, measuring levels thereof in appropriate physiological samples (by immunoassay), in diagnostic methods, etc. This hold true also for a derivative, or homologue thereof of a complex.

In another embodiment of the invention (see *infra*), an antibody to a complex or a fragment of such antibodies containing the antibody binding domain, is a therapeutic.

4.3 DIAGNOSTIC, PROGNOSTIC, AND SCREENING USES OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The particular protein complexes and proteins of the present invention may be markers of normal physiological processes, and thus have diagnostic utility. Further, definition of particular groups of patients with elevations or deficiencies of a protein complex of the present invention, or wherein the protein complex has a change in protein component composition, can lead to new nosological classifications of diseases, furthering diagnostic ability.

Examples for diseases or disorders are neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.

Detecting levels of protein complexes, or individual component proteins that form the complexes, or detecting levels of the mRNAs encoding the components of the complex, may be used in diagnosis, prognosis, and/or staging to follow the course of a disease state, to follow a therapeutic response, etc.

A protein complex of the present invention and the individual components of the complex and a derivative, analog or subsequence thereof, encoding nucleic acids (and sequences complementary thereto), and anti-complex antibodies and antibodies directed against individual components that can form the complex, are useful in diagnostics. The foregoing molecules can be used in assays, such as immunoassays, to detect, prognose, diagnose, or monitor various conditions, diseases, and disorders characterized by aberrant levels of a complex or aberrant component composition of a complex, or monitor the treatment of such various conditions, diseases, and disorders.

In particular, such an immunoassay is carried out by a method comprising contacting a sample derived from a patient with an anti-complex antibody under conditions such that immunospecific binding can occur, and detecting or measuring the amount of any immunospecific binding by the antibody. In a specific aspect, such binding of antibody, in tissue sections, can be used to detect aberrant complex localization, or aberrant (e.g., high, low or absent) levels of a protein complex or complexes. In a specific embodiment, an antibody to the complex can be used to assay a patient tissue or serum sample for the presence of the complex, where an aberrant level of the complex is an indication of a diseased condition. By "aberrant levels" is meant increased or decreased levels relative to that present, or a standard level representing that present, in an analogous sample from a portion or fluid of the body, or from a subject not having the disorder.

The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as Western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few known in the art.

Nucleic acids encoding the components of the protein complex and related nucleic acid sequences and subsequences, including complementary sequences, can be used in hybridization assays. The nucleic acid sequences, or subsequences thereof,

comprising about at least 8 nucleotides, can be used as hybridization probes. Hybridization assays can be used to detect, prognose, diagnose, or monitor conditions, disorders, or disease states associated with aberrant levels of the mRNAs encoding the components of a complex as described, supra. In particular, such a hybridization assay is carried out by a method comprising contacting a sample containing nucleic acid with a nucleic acid probe capable of hybridizing to component protein coding DNA or RNA, under conditions such that hybridization can occur, and detecting or measuring any resulting hybridization.

In specific embodiments, diseases and disorders involving or characterized by aberrant levels of a protein complex or aberrant complex composition can be diagnosed, or its suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by determining the component protein composition of the complex, or detecting aberrant levels of a member of the complex or un-complexed component proteins or encoding nucleic acids, or functional activity including, but not restricted to, binding to an interacting partner, or by detecting mutations in component protein RNA, DNA or protein (e.g., mutations such as translocations, truncations, changes in nucleotide or amino acid sequence relative to wild-type that cause increased or decreased expression or activity of a complex, and/or component protein).

Such diseases and disorders include, but are not limited to neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.

By way of example, levels of a protein complex and the individual components of a complex can be detected by immunoassay, levels of component protein RNA or DNA can be detected by hybridization assays (e.g., Northern blots, dot blots, RNase protection assays), and binding of component proteins to each other (e.g., complex formation) can be measured by binding assays commonly known in the art. Translocations and point mutations in component protein genes can be detected by Southern blotting, RFLP analysis, PCR using primers that preferably generate a fragment spanning at least most of the gene by sequencing of genomic DNA or cDNA obtained from the patient, etc.

Assays well known in the art (e.g., assays described above such as immunoassays, nucleic acid hybridization assays, activity assays, etc.) can be used to determine whether one or more particular protein complexes are present at either increased or decreased levels, or are absent, in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or

disorder, as compared to the levels in samples from subjects not having such a disease or disorder, or having a predisposition to develop such a disease or disorder. Additionally, these assays can be used to determine whether the ratio of the complex to the un-complexed components of the complex, is increased or decreased in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the ratio in samples from subjects not having such a disease or disorder.

In the event that levels of one or more particular protein complexes (i.e., complexes formed from component protein derivatives, homologs, fragments, or analogs) are determined to be increased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder, or predisposition for a disease or disorder, can be diagnosed, have prognosis defined for, be screened for, or be monitored by detecting increased levels of the one or more protein complexes, increased levels of the mRNA that encodes one or more members of the one or more particular protein complexes, or by detecting increased complex functional activity.

Accordingly, in a specific embodiment of the present invention, diseases and disorders involving increased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting increased levels of the one or more protein complexes, the mRNA encoding both members of the complex, or complex functional activity, or by detecting mutations in the component proteins that stabilize or enhance complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that stabilize or enhance complex formation.

In the event that levels of one or more particular protein complexes are determined to be decreased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder or predisposition for a disease or disorder can be diagnosed, have its prognosis determined, be screened for, or be monitored by detecting decreased levels of the one or more protein complexes, the mRNA that encodes one or more members of the particular one or more protein complexes, or by detecting decreased protein complex functional activity.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving decreased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting decreased levels of the one or more protein complexes, the mRNA encoding one or more members of the one or more complexes, or complex functional activity, or by detecting mutations in the component proteins that decrease complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that decrease complex formation.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving aberrant compositions of the complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting the component proteins of one or more complexes, or the mRNA encoding the members of the one or more complexes.

The use of detection techniques, especially those involving antibodies against a protein complex, provides a method of detecting specific cells that express the complex or component proteins. Using such assays, specific cell types can be defined in which one or more particular protein complexes are expressed, and the presence of the complex or component proteins can be correlated with cell viability, state, health, etc.

Also embodied are methods to detect a protein complex of the present invention in cell culture models that express particular protein complexes or derivatives thereof, for the purpose of characterizing or preparing the complexes for harvest. This embodiment includes cell sorting of prokaryotes such as but not restricted to bacteria (Davey and Kell, 1996, *Microbiol. Rev.* 60:641-696), primary cultures and tissue specimens from eukaryotes, including mammalian species such as human (Steele et al., 1996, *Clin. Obstet. Gynecol.* 39:801-813), and continuous cell cultures (Orfao and Ruiz-Arguelles, 1996, *Clin. Biochem.* 29:5-9). Such isolations can be used as methods of diagnosis, described, *supra*.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

4.4 THERAPEUTIC USES OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The present invention is directed to a method for treatment or prevention of various diseases and disorders by administration of a therapeutic compound (termed herein "therapeutic"). Such "therapeutics" include, but are not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments) of the foregoing (e.g., as described hereinabove); antibodies thereto (as described hereinabove); nucleic acids encoding the component

protein, and analogs or derivatives, thereof (e.g., as described hereinabove); component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The protein complexes as identified herein can be implicated in processes which are implicated in or associated with pathological conditions.

Diseases and disorders which can be treated and/or prevented and/or diagnosed by therapeutics interacting with any of the complexes provided herein are for example neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders, inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease.

These disorders are treated or prevented by administration of a therapeutic that modulates (i.e. inhibits or promotes) protein complex activity or formation or modulates its function or composition. Diseases or disorders associated with aberrant levels of complex activity or formation, or aberrant levels or activity of the component proteins, or aberrant complex composition or a change in the function, may be treated by administration of a therapeutic that modulates complex formation or activity or by the administration of a protein complex.

Therapeutics may also be administered to modulate complex formation or activity or level thereof in a microbial organism such as yeast, fungi such as candida albicans causing an infectious disease in animals or humans.

Diseases and disorders characterized by increased (relative to a subject not suffering from the disease or disorder) complex levels or activity can be treated with therapeutics that antagonize (i.e., reduce or inhibit) complex formation or activity. Therapeutics that can be used include, but are not limited to, the component proteins or an analog, derivative or fragment of the component protein; anti-complex antibodies (e.g., antibodies specific for the protein complex, or a fragment or derivative of the antibody containing the binding region thereof; nucleic acids encoding the component proteins; antisense nucleic acids complementary to nucleic acids encoding the component proteins; and nucleic acids encoding the component protein that are dysfunctional due to, e.g., a heterologous insertion within the protein coding sequence, that are used to "knockout" endogenous protein function by homologous recombination, see, e.g., Capecchi, 1989, Science 244:1288-1292. In one embodiment, a therapeutic is 1, 2 or more antisense nucleic acids which are complementary to 1, 2, or more nucleic acids, respectively, that encode component proteins of a complex.

In a specific embodiment of the present invention, a nucleic acid containing a portion of a component protein gene in which gene sequences flank (are both 5' and 3' to) a different gene sequence, is used as a component protein antagonist, or to promote component protein inactivation by homologous recombination (see also, Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342: 435-438). Additionally, mutants or derivatives of a component protein that has greater affinity for another component protein or the complex than wild type may be administered to compete with wild type protein for binding, thereby reducing the levels of complexes containing the wild type protein. Other therapeutics that inhibit complex function can be identified by use of known convenient in vitro assays, e.g., based on their ability to inhibit complex formation, or as described in Section 4.5, *infra*.

In specific embodiments, therapeutics that antagonize complex formation or activity are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an increased (relative to normal or desired) level of a complex, for example, in patients where complexes are overactive or overexpressed; or (2) in diseases or disorders where an in vitro (or in vivo) assay (see *infra*) indicates the utility of antagonist administration. Increased levels of a complex can be readily detected, e.g., by quantifying protein and/or RNA, by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, or structure and/or activity of the expressed complex (or the encoding mRNA). Many methods standard in the art can be thus employed including, but not limited to, immunoassays to detect complexes and/or visualize complexes (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.), and/or hybridization assays to detect concurrent expression of component protein mRNA (e.g., Northern assays, dot blot analysis, in situ hybridization, etc.).

A more specific embodiment of the present invention is directed to a method of reducing complex expression (i.e., expression of the protein components of the complex and/or formation of the complex) by targeting mRNAs that express the protein moieties. RNA therapeutics currently fall within three classes, antisense species, ribozymes, or RNA aptamers (Good et al., 1997, *Gene Therapy* 4:45-54).

Antisense oligonucleotides have been the most widely used. By way of example, but not limitation, antisense oligonucleotide methodology to reduce complex formation is presented below, *infra*. Ribozyme therapy involves the administration, induced

expression, etc. of small RNA molecules with enzymatic ability to cleave, bind, or otherwise inactivate specific RNAs, to reduce or eliminate expression of particular proteins (Grassi and Marini, 1996, *Annals of Medicine* 28:499-510; Gibson, 1996, *Cancer and Metastasis Reviews* 15:287-299). RNA aptamers are specific RNA ligand proteins, such as for Tat and Rev RNA (Good et al., 1997, *Gene Therapy* 4:45-54) that can specifically inhibit their translation. Aptamers specific for component proteins can be identified by many methods well known in the art, for example, by affecting the formation of a complex in the protein-protein interaction assay described, *infra*.

In another embodiment, the activity or levels of a component protein are reduced by administration of another component protein, or the encoding nucleic acid, or an antibody that immunospecifically binds to the component protein, or a fragment or a derivative of the antibody containing the binding domain thereof.

In another aspect of the invention, diseases or disorders associated with increased levels of a component protein of the complex may be treated or prevented by administration of a therapeutic that increases complex formation if the complex formation acts to reduce or inactivate the component protein through complex formation. Such diseases or disorders can be treated or prevented by administration of one component member of the complex, administration of antibodies or other molecules that stabilize the complex, etc.

Diseases and disorders associated with underexpression of a complex, or a component protein, are treated or prevented by administration of a therapeutic that promotes (i.e., increases or supplies) complex levels and/or function, or individual component protein function. Examples of such a therapeutic include but are not limited to a complex or a derivative, analog or fragment of the complex that are functionally active (e.g., able to form a complex), un-complexed component proteins and derivatives, analogs, and fragments of un-complexed component proteins, and nucleic acids encoding the members of a complex or functionally active derivatives or fragments of the members of the complex, e.g., for use in gene therapy. In a specific embodiment, a therapeutic includes derivatives, homologs or fragments of a component protein that increase and/or stabilize complex formation. Examples of other agonists can be identified using *in vitro* assays or animal models, examples of which are described, *infra*.

In yet other specific embodiments of the present invention, therapeutics that promote complex function are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an absence or decreased (relative to normal or

desired) level of a complex, for example, in patients where a complex, or the individual components necessary to form the complex, is lacking, genetically defective, biologically inactive or underactive, or under-expressed; or (2) in diseases or disorders wherein an in vitro or in vivo assay (see, infra) indicates the utility of complex agonist administration. The absence or decreased level of a complex, component protein or function can be readily detected, e.g., by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, structure and/or activity of the expressed complex and/or the concurrent expression of mRNA encoding the two components of the complex. Many methods standard in the art can be thus employed, including but not limited to immunoassays to detect and/or visualize a complex, or the individual components of a complex (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs encoding the individual protein components of a complex by detecting and/or visualizing component mRNA concurrently or separately using, e.g., Northern assays, dot blot analysis, in situ hybridization, etc.

In specific embodiments, the activity or levels of a component protein are increased by administration of another component protein of the same complex, or a derivative, homolog or analog thereof, a nucleic acid encoding the other component, or an agent that stabilizes or enhances the other component, or a fragment or derivative of such an agent.

Generally, administration of products of species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, a human complex, or derivative, homolog or analog thereof; nucleic acids encoding the members of the human complex or a derivative, homolog or analog thereof; an antibody to a human complex, or a derivative thereof; or other human agents that affect component proteins or the complex, are therapeutically or prophylactically administered to a human patient.

Preferably, suitable in vitro or in vivo assays are utilized to determine the effect of a specific therapeutic and whether its administration is indicated for treatment of the affected tissue or individual.

In various specific embodiments, in vitro assays can be carried out with representative cells of cell types involved in a patient's disorder, to determine if a therapeutic has a desired effect upon such cell types.

Compounds for use in therapy can be tested in suitable animal model systems prior to testing in humans, including, but not limited to, rats, mice, chicken, cows, monkeys, rabbits, etc. For in vivo testing, prior to administration to humans, any animal model system known in the art may be used. Additional descriptions and sources of therapeutics that can be used according to the invention are found in Sections 4.1 to 4.3 and 4.7 herein.

4.4.1 GENE THERAPY

In a specific embodiment of the present invention, nucleic acids comprising a sequence encoding the component proteins, or a functional derivative thereof, are administered to modulate complex activity or formation by way of gene therapy. Gene therapy refers to therapy performed by the administration of a nucleic acid to a subject. In this embodiment of the present invention, the nucleic acid expresses its encoded protein(s) that mediates a therapeutic effect by modulating complex activity or formation. Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, *Clinical Pharmacy* 12:488-505; Wu and Wu, 1991, *Biotherapy* 3:87-95; Tolstoshev, 1993, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596; Mulligan, 1993, *Science* 260:926-932; Morgan and Anderson, 1993, *Ann. Rev. Biochem.* 62:191-217; and May, 1993, *TIBTECH* 11:155-215. Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al., eds., 1993, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY; and Kriegler, 1990, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY.

In a preferred aspect, the therapeutic comprises a nucleic acid that is part of an expression vector that expresses one or more of the component proteins, or fragments or chimeric proteins thereof, in a suitable host. In particular, such a nucleic acid has a promoter operably linked to the protein coding region(s) (or, less preferably separate promoters linked to the separate coding regions separately), said promoter being inducible or constitutive, and optionally, tissue-specific. In another particular embodiment, a nucleic acid molecule is used in which the coding sequences, and any other desired sequences, are flanked by regions that promote homologous

recombination at a desired site in the genome, thus providing for intra-chromosomal expression of the component protein nucleic acids (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

Delivery of the nucleic acid into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vector, or indirect, in which case, cells are first transformed with the nucleic acid in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid is directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by infection using a defective or attenuated retroviral or other viral vector (U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors, or through use of transfecting agents, by encapsulation in liposomes, microparticles, or microcapsules, or by administering it in linkage to a peptide that is known to enter the nucleus, or by administering it in linkage to a ligand subject to receptor-mediated endocytosis that can be used to target cell types specifically expressing the receptors (e.g., Wu and Wu, 1987, J. Biol. Chem. 262:4429-4432), etc. In another embodiment, a nucleic acid-ligand complex can be formed in which the ligand comprises a fusogenic viral peptide that disrupts endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., International Patent Publications WO 92/06180; WO 92/22635; WO 92/20316; WO 93/14188; and WO 93/20221. Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

In a specific embodiment, a viral vector that contains the component protein encoding nucleic acids is used. For example, a retroviral vector can be used (Miller et al., 1993, Meth. Enzymol. 217:581-599). These retroviral vectors have been modified to delete retroviral sequences that are not necessary for packaging of the viral genome and integration into host cell DNA. The encoding nucleic acids to be used in gene therapy

is/are cloned into the vector, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., 1994, *Biotherapy* 6:291-302, which describes the use of a retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are Clowes et al., 1994, *J. Clin. Invest.* 93:644-651; Kiem et al., 1994, *Blood* 83:1467-1473; Salmons and Gunzberg, 1993, *Human Gene Therapy* 4:129-141; and Grossman and Wilson, 1993, *Curr. Opin. in Genetics and Devel.* 3:110-114.

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are the liver, the central nervous system, endothelial cells and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, 1993, *Curr. Opin. Genet. Devel.* 3:499-503, discuss adenovirus-based gene therapy. The use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys has been demonstrated by Bout et al., 1994, *Human Gene Therapy* 5:3-10. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., 1991, *Science* 252:431-434; Rosenfeld et al., 1992, *Cell* 68:143-155; and Mastrangeli et al., 1993, *J. Clin. Invest.* 91:225-234.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., 1993, *Proc. Soc. Exp. Biol. Med.* 204:289-300).

Another approach to gene therapy involves transferring a gene into cells in tissue culture by methods such as electroporation, lipofection, calcium phosphate-mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene from those that have not. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art including, but not limited to, transfection by electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the

introduction of foreign genes into cells (see, e.g., Loeffler and Behr, 1993, *Meth. Enzymol.* 217:599-618; Cohen et al., 1993, *Meth. Enzymol.* 217:618-644; Cline, 1985, *Pharmac. Ther.* 29:69-92) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably, is heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. In a preferred embodiment, epithelial cells are injected, e.g., subcutaneously. In another embodiment, recombinant skin cells may be applied as a skin graft onto the patient. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes, blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, and granulocytes, various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, a component protein encoding nucleic acid is/are introduced into the cells such that the gene or genes are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention. Such stem cells include but are not limited to hematopoietic stem cells (HSCs), stem cells of epithelial tissues such as the skin and the lining of the gut, embryonic heart muscle cells, liver stem cells (International Patent Publication WO 94/08598), and neural stem cells (Stemple and Anderson, 1992, *Cell* 71:973-985).

Epithelial stem cells (ESCs), or keratinocytes, can be obtained from tissues such as the skin and the lining of the gut by known procedures (Rheinwald, 1980, *Meth. Cell Biol.* 2A:229). In stratified epithelial tissue such as the skin, renewal occurs by mitosis of stem cells within the germinal layer, the layer closest to the basal lamina. Similarly, stem cells within the lining of the gut provide for a rapid renewal rate of this tissue. ESCs or keratinocytes obtained from the skin or lining of the gut of a patient or donor can be grown in tissue culture (Rheinwald, 1980, *Meth. Cell Bio.* 2A:229; Pittelkow and Scott, 1986, *Mayo Clinic Proc.* 61:771). If the ESCs are provided by a donor, a method for suppression of host versus graft reactivity (e.g., irradiation, or drug or antibody administration to promote moderate immunosuppression) can also be used.

With respect to hematopoietic stem cells (HSCs), any technique that provides for the isolation, propagation, and maintenance in vitro of HSCs can be used in this embodiment of the invention. Techniques by which this may be accomplished include (a) the isolation and establishment of HSC cultures from bone marrow cells isolated from the future host, or a donor, or (b) the use of previously established long-term HSC cultures, which may be allogeneic or xenogeneic. Non-autologous HSCs are used preferably in conjunction with a method of suppressing transplantation immune reactions between the future host and patient. In a particular embodiment of the present invention, human bone marrow cells can be obtained from the posterior iliac crest by needle aspiration (see, e.g., Kodo et al., 1984, *J. Clin. Invest.* 73: 1377-1384). In a preferred embodiment of the present invention, the HSCs can be made highly enriched or in substantially pure form. This enrichment can be accomplished before, during, or after long-term culturing, and can be done by any technique known in the art. Long-term cultures of bone marrow cells can be established and maintained by using, for example, modified Dexter cell culture techniques (Dexter et al., 1977, *J. Cell Physiol.* 91:335) or Witlock-Witte culture techniques (Witlock and Witte, 1982, *Proc. Natl. Acad. Sci. USA* 79:3608-3612).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

Additional methods can be adapted for use to deliver a nucleic acid encoding the component proteins, or functional derivatives thereof, e.g., as described in Section 4.1, *supra*.

4.4.2 USE OF ANTISENSE OLIGONUCLEOTIDES FOR SUPPRESSION OF PROTEIN COMPLEX FORMATION OR PROTEIN COMPLEX/PROTEIN ACTIVITY

In a specific embodiment of the present invention, protein complex activity and formation and protein activity is inhibited by use of antisense nucleic acids for the component proteins of the complex, that inhibit transcription and/or translation of their complementary sequence. The present invention provides the therapeutic or prophylactic use of nucleic acids of at least six nucleotides that are antisense to a gene or cDNA encoding a component protein, or a portion thereof. An "antisense" nucleic acid as used herein refers to a nucleic acid capable of hybridizing to a sequence-specific portion of a component protein RNA (preferably mRNA) by virtue of some sequence complementarity. The antisense nucleic acid may be complementary to a coding and/or noncoding region of a component protein mRNA. Such antisense nucleic acids that inhibit complex formation or activity have utility as therapeutics, and can be used in the treatment or prevention of disorders as described supra.

The antisense nucleic acids of the invention can be oligonucleotides that are double-stranded or single-stranded, RNA or DNA, or a modification or derivative thereof, which can be directly administered to a cell, or which can be produced intracellularly by transcription of exogenous, introduced sequences.

In another embodiment, the present invention is directed to a method for inhibiting the expression of component protein nucleic acid sequences, in a prokaryotic or eukaryotic cell, comprising providing the cell with an effective amount of a composition comprising an antisense nucleic acid of the component protein, or a derivative thereof, of the invention.

The antisense nucleic acids are of at least six nucleotides and are preferably oligonucleotides, ranging from 6 to about 200 nucleotides. In specific aspects, the oligonucleotide is at least 10 nucleotides, at least 15 nucleotides, at least 100 nucleotides, or at least 200 nucleotides. The oligonucleotides can be DNA or RNA or chimeric mixtures, or derivatives or modified versions thereof, and either single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents facilitating transport across the cell membrane (see,

e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. USA 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. USA 84:648-652; International Patent Publication No. WO 88/09810) or blood-brain barrier (see, e.g., International Patent Publication No. WO 89/10134), hybridization-triggered cleavage agents (see, e.g., Krol et al., 1988, BioTechniques 6:958-976), or intercalating agents (see, e.g., Zon, 1988, Pharm. Res. 5:539-549).

In a preferred aspect of the invention, an antisense oligonucleotide is provided, preferably as single-stranded DNA. The oligonucleotide may be modified at any position in its structure with constituents generally known in the art.

The antisense oligonucleotides may comprise at least one modified base moiety which is selected from the group including but not limited to 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl)uracil, 5-carboxymethylaminomethyl-2-thio-uridine, 5-carboxymethylaminomethyluracil, dihydrouracil, β -D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, β -D-mannosylqueosine, 5N-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methyl-thio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

In another embodiment, the oligonucleotide comprises at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the oligonucleotide comprises at least one modified phosphate backbone selected from the group consisting of a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal, or an analog of the foregoing.

In yet another embodiment, the oligonucleotide is a 2-a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641).

The oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization-triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

Oligonucleotides of the invention may be synthesized by standard methods known in the art, e.g., by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligo-nucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. USA 85:7448-7451), etc.

In a specific embodiment, the antisense oligonucleotides comprise catalytic RNAs, or ribozymes (see, e.g., International Patent Publication No. WO 90/11364; Sarver et al., 1990, Science 247:1222-1225). In another embodiment, the oligonucleotide is a 2'-O-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analog (Inoue et al., 1987, FEBS Lett. 215:327-330).

In an alternative embodiment, the antisense nucleic acids of the invention are produced intracellularly by transcription from an exogenous sequence. For example, a vector can be introduced in vivo such that it is taken up by a cell, within which cell the vector or a portion thereof is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the component protein. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art to be capable of replication and expression in mammalian cells. Expression of the sequences encoding the antisense RNAs can be by any promoter known in the art to act in mammalian, preferably human, cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., 1980, Cell 22:787-797); the herpes thymidine kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. USA 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, Nature 296:39-42), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a component protein gene, preferably a human gene. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," as referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with a component protein RNA it may contain and still form a stable duplex (or triplex, as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

The component protein antisense nucleic acids can be used to treat (or prevent) disorders of a cell type that expresses, or preferably overexpresses, a protein complex.

Cell types that express or overexpress component protein RNA can be identified by various methods known in the art. Such methods include, but are not limited to, hybridization with component protein-specific nucleic acids (e.g., by Northern blot hybridization, dot blot hybridization, or in situ hybridization), or by observing the ability of RNA from the cell type to be translated in vitro into the component protein by immunohistochemistry, Western blot analysis, ELISA, etc. In a preferred aspect, primary tissue from a patient can be assayed for protein expression prior to treatment, e.g., by immunocytochemistry, in situ hybridization, or any number of methods to detect protein or mRNA expression.

Pharmaceutical compositions of the invention (see Section 4.7, *infra*), comprising an effective amount of a protein component antisense nucleic acid in a pharmaceutically acceptable carrier can be administered to a patient having a disease or disorder that is of a type that expresses or overexpresses a protein complex of the present invention.

The amount of antisense nucleic acid that will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. Where possible, it is desirable to determine the antisense cytotoxicity in vitro, and then in useful animal model systems, prior to testing and use in humans.

In a specific embodiment, pharmaceutical compositions comprising antisense nucleic acids are administered via liposomes, microparticles, or microcapsules. In various embodiments of the invention, it may be useful to use such compositions to achieve sustained release of the antisense nucleic acids. In a specific embodiment, it may be desirable to utilize liposomes targeted via antibodies to specific identifiable central nervous system cell types (Leonetti et al., 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2448-2451; Renneisen et al., 1990, J. Biol. Chem. 265:16337-16342).

4.5 ASSAYS OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION AND DERIVATIVES AND ANALOGS THEREOF

The functional activity of a protein complex of the present invention, or a derivative, fragment or analog thereof or protein component thereof, can be assayed by various methods. Potential modulators (e.g., agonists and antagonists) of complex activity or formation, e.g., anti-complex antibodies and antisense nucleic acids, can be assayed for the ability to modulate complex activity or formation.

In one embodiment of the present invention, where one is assaying for the ability to bind or compete with a wild-type complex for binding to an anti-complex antibody, various immunoassays known in the art can be used, including but not limited to competitive and non-competitive assay systems using techniques such as radioimmunoassay, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitin reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels), western blot analysis, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

The expression of the component protein genes (both endogenous and those expressed from cloned DNA containing the genes) can be detected using techniques

known in the art, including but not limited to Southern hybridization (Southern, 1975, J. Mol. Biol. 98:503-517), northern hybridization (see, e.g., Freeman et al., 1983, Proc. Natl. Acad. Sci. USA 80:4094-4098), restriction endonuclease mapping (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2nd Ed. Cold Spring Harbor Laboratory Press, New York), RNase protection assays (Current Protocols in Molecular Biology, John Wiley and Sons, New York, 1997), DNA sequence analysis, and polymerase chain reaction amplification (PCR; U.S. Patent Nos. 4,683,202, 4,683,195, and 4,889,818; Gyllenstein et al., 1988, Proc. Natl. Acad. Sci. USA 85:7652-7657; Ochman et al., 1988, Genetics 120:621-623; Loh et al., 1989, Science 243:217-220) followed by Southern hybridization with probes specific for the component protein genes, in various cell types. Methods of amplification other than PCR commonly known in the art can be employed. In one embodiment, Southern hybridization can be used to detect genetic linkage of component protein gene mutations to physiological or pathological states. Various cell types, at various stages of development, can be characterized for their expression of component proteins at the same time and in the same cells. The stringency of the hybridization conditions for northern or Southern blot analysis can be manipulated to ensure detection of nucleic acids with the desired degree of relatedness to the specific probes used. Modifications to these methods and other methods commonly known in the art can be used.

Derivatives (e.g., fragments), homologs and analogs of one component protein can be assayed for binding to another component protein in the same complex by any method known in the art, for example the modified yeast matrix mating test described in Section 4.6.1 *infra*, immunoprecipitation with an antibody that binds to the component protein complexed with other component proteins in the same complex, followed by size fractionation of the immunoprecipitated proteins (e.g., by denaturing or nondenaturing polyacrylamide gel electrophoresis), Western blot analysis, etc.

One embodiment of the invention provides a method for screening a derivative, homolog or analog of a component protein for biological activity comprising contacting said derivative, homolog or analog of the component protein with the other component proteins in the same complex; and detecting the formation of a complex between said derivative, homolog or analog of the component protein and the other component proteins; wherein detecting formation of said complex indicates that said derivative, homolog or analog of has biological (e.g., binding) activity.

The invention also provides methods of modulating the activity of a component protein that can participate in a protein complex by administration of a binding partner of that protein or derivative, homolog or analog thereof.

In a specific embodiment of the present invention, a protein complex of the present invention is administered to treat or prevent a disease or disorder, since the complex and/or component proteins have been implicated in the disease and disorder. Accordingly, a protein complex or a derivative, homolog, analog or fragment thereof, nucleic acids encoding the component proteins, anti-complex antibodies, and other modulators of protein complex activity, can be tested for activity in treating or preventing a disease or disorder in in vitro and in vivo assays.

In one embodiment, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by contacting cultured cells that exhibit an indicator of the disease in vitro, with the therapeutic, and comparing the level of said indicator in the cells contacted with the therapeutic, with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the therapeutic has activity in treating or preventing the disease.

In another embodiment of the invention, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by administering the therapeutic to a test animal that is predisposed to develop symptoms of a disease, and measuring the change in said symptoms of the disease after administration of said therapeutic, wherein a reduction in the severity of the symptoms of the disease or prevention of the symptoms of the disease indicates that the therapeutic has activity in treating or preventing the disease. Such a test animal can be any one of a number of animal models known in the art for disease. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention.

4.6 SCREENING FOR MODULATORS OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

A complex of the present invention, the component proteins of the complex and nucleic acids encoding the component proteins, as well as derivatives and fragments of the amino and nucleic acids, can be used to screen for compounds that bind to, or

modulate the amount of, activity of, or protein component composition of, said complex, and thus, have potential use as modulators, i.e., agonists or antagonists, of complex activity, and/or complex formation, i.e., the amount of complex formed, and/or protein component composition of the complex.

Thus, the present invention is also directed to methods for screening for molecules that bind to, or modulate the function of, amount of, activity of, formation of or protein component composition of, a complex of the present invention. In one embodiment of the invention, the method for screening for a molecule that modulates directly or indirectly the function, activity or formation of a complex of the present invention comprises exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules under conditions conducive to modulation; and determining the amount of, the biochemical activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependend on the complex and/or the abundance and/or activity of a protein or protein complex dependend on the function of the complex and/or product of a gene dependend on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependend on the complex and/or the abundance and/or activity of a protein or protein complex dependend on the function of the complex and/or product of a gene dependend on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

In another embodiment, the present invention further relates to a process for the identification and/or preparation of an effector of the complex comprising the step of bringing into contact a product of any of claims 1 to 8 with a compound, a mixture or a library of compounds and determining whether the compound or a certain compound of the mixture or library binds to the product and/or effects the products biological activity and optionally further purifying the compound positively tested as effector.

In another embodiment, the present invention is directed to a method for screening for a molecule that binds a protein complex of the present invention comprising exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules; and determining whether said complex is bound by any of said candidate molecules. Such screening assays can be carried out using cell-free and cell-based methods that are commonly known in the art in vitro, in vivo or ex vivo. For example, an isolated complex can be employed, or a cell can be contacted with the candidate molecule and the complex can be isolated from such contacted cells and the isolated complex can be assayed for activity or component composition. In another example, a cell containing the complex can be contacted with

the candidate molecule and the levels of the complex in the contacted cell can be measured. Additionally, such assays can be carried out in cells recombinantly expressing a component protein from the third column of table 1, or a functionally active fragment or functionally active derivative thereof, and a component protein from fourth column of table 1, or a functionally active fragment or functionally active derivative thereof. Additionally, such assays can also be carried out in cells recombinantly expressing all component proteins from the group of proteins in the fifth column of table 1.

For example, assays can be carried out using recombinant cells expressing the protein components of a complex, to screen for molecules that bind to, or interfere with, or promote complex activity or formation. In preferred embodiments, polypeptide derivatives that have superior stabilities but retain the ability to form a complex (e.g., one or more component proteins modified to be resistant to proteolytic degradation in the binding assay buffers, or to be resistant to oxidative degradation), are used to screen for modulators of complex activity or formation. Such resistant molecules can be generated, e.g., by substitution of amino acids at proteolytic cleavage sites, the use of chemically derivatized amino acids at proteolytic susceptible sites, and the replacement of amino acid residues subject to oxidation, i.e. methionine and cysteine.

A particular aspect of the present invention relates to identifying molecules that inhibit or promote formation or degradation of a complex of the present invention, e.g., using the method described for isolating the complex and identifying members of the complex using the TAP assay described in Section 4, *infra*, and in WO 00/09716 and Rigaut et al., 1999, *Nature Biotechnol.* 17:1030-1032, which are each incorporated by reference in their entirety. TNRF1

In another embodiment of the invention, a modulator is identified by administering a candidate molecule to a transgenic non-human animal expressing the complex component proteins from promoters that are not the native promoters of the respective proteins, more preferably where the candidate molecule is also recombinantly expressed in the transgenic non-human animal. Alternatively, the method for identifying such a modulator can be carried out *in vitro*, preferably with a purified complex, and a purified candidate molecule.

Agents/molecules (candidate molecules) to be screened can be provided as mixtures of a limited number of specified compounds, or as compound libraries, peptide libraries and the like. Agents/molecules to be screened may also include all forms of

antisera, antisense nucleic acids, etc., that can modulate complex activity or formation. Exemplary candidate molecules and libraries for screening are set forth in Section 4.6.1, *infra*.

Screening the libraries can be accomplished by any of a variety of commonly known methods. See, e.g., the following references, which disclose screening of peptide libraries: Parmley and Smith, 1989, *Adv. Exp. Med. Biol.* 251:215-218; Scott and Smith, 1990, *Science* 249:386-390; Fowlkes et al., 1992, *BioTechniques* 13:422-427; Oldenburg et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:5393-5397; Yu et al., 1994, *Cell* 76:933-945; Staudt et al., 1988, *Science* 241:577-580; Bock et al., 1992, *Nature* 355:564-566; Tuerk et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:6988-6992; Ellington et al., 1992, *Nature* 355:850-852; U.S. Patent No. 5,096,815, U.S. Patent No. 5,223,409, and U.S. Patent No. 5,198,346, all to Ladner et al.; Rebar and Pabo, 1993, *Science* 263:671-673; and International Patent Publication No. WO 94/18318.

In a specific embodiment, screening can be carried out by contacting the library members with a complex immobilized on a solid phase, and harvesting those library members that bind to the protein (or encoding nucleic acid or derivative). Examples of such screening methods, termed "panning" techniques, are described by way of example in Parmley and Smith, 1988, *Gene* 73:305-318; Fowlkes et al., 1992, *BioTechniques* 13:422-427; International Patent Publication No. WO 94/18318; and in references cited hereinabove.

In a specific embodiment, fragments and/or analogs of protein components of a complex, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex formation (amount of complex or composition of complex) or activity in the cell, which thereby inhibit complex activity or formation in the cell.

In one embodiment, agents that modulate (i.e., antagonize or agonize) complex activity or formation can be screened for using a binding inhibition assay, wherein agents are screened for their ability to modulate formation of a complex under aqueous, or physiological, binding conditions in which complex formation occurs in the absence of the agent to be tested. Agents that interfere with the formation of complexes of the invention are identified as antagonists of complex formation. Agents that promote the formation of complexes are identified as agonists of complex formation. Agents that completely block the formation of complexes are identified as inhibitors of complex formation.

Methods for screening may involve labeling the component proteins of the complex with radioligands (e.g., ^{125}I or ^3H), magnetic ligands (e.g., paramagnetic beads covalently attached to photobiotin acetate), fluorescent ligands (e.g., fluorescein or rhodamine), or enzyme ligands (e.g., luciferase or β -galactosidase). The reactants that bind in solution can then be isolated by one of many techniques known in the art, including but not restricted to, co-immunoprecipitation of the labeled complex moiety using antisera against the unlabeled binding partner (or labeled binding partner with a distinguishable marker from that used on the second labeled complex moiety), immunoaffinity chromatography, size exclusion chromatography, and gradient density centrifugation. In a preferred embodiment, the labeled binding partner is a small fragment or peptidomimetic that is not retained by a commercially available filter. Upon binding, the labeled species is then unable to pass through the filter, providing for a simple assay of complex formation.

Methods commonly known in the art are used to label at least one of the component members of the complex. Suitable labeling methods include, but are not limited to, radiolabeling by incorporation of radiolabeled amino acids, e.g., ^3H -leucine or ^{35}S -methionine, radiolabeling by post-translational iodination with ^{125}I or ^{131}I using the chloramine T method, Bolton-Hunter reagents, etc., or labeling with ^{32}P using phosphorylase and inorganic radiolabeled phosphorous, biotin labeling with photobiotin-acetate and sunlamp exposure, etc. In cases where one of the members of the complex is immobilized, e.g., as described *infra*, the free species is labeled. Where neither of the interacting species is immobilized, each can be labeled with a distinguishable marker such that isolation of both moieties can be followed to provide for more accurate quantification, and to distinguish the formation of homomeric from heteromeric complexes. Methods that utilize accessory proteins that bind to one of the modified interactants to improve the sensitivity of detection, increase the stability of the complex, etc., are provided.

Typical binding conditions are, for example, but not by way of limitation, in an aqueous salt solution of 10-250 mM NaCl, 5-50 mM Tris-HCl, pH 5-8, and 0.5% Triton X-100 or other detergent that improves specificity of interaction. Metal chelators and/or divalent cations may be added to improve binding and/or reduce proteolysis. Reaction temperatures may include 4, 10, 15, 22, 25, 35, or 42 degrees Celsius, and time of incubation is typically at least 15 seconds, but longer times are preferred to allow binding

equilibrium to occur. Particular complexes can be assayed using routine protein binding assays to determine optimal binding conditions for reproducible binding.

The physical parameters of complex formation can be analyzed by quantification of complex formation using assay methods specific for the label used, e.g., liquid scintillation counting for radioactivity detection, enzyme activity for enzyme-labeled moieties, etc. The reaction results are then analyzed utilizing Scatchard analysis, Hill analysis, and other methods commonly known in the arts (see, e.g., *Proteins, Structures, and Molecular Principles*, 2nd Edition (1993) Creighton, Ed., W.H. Freeman and Company, New York).

In a second common approach to binding assays, one of the binding species is immobilized on a filter, in a microtiter plate well, in a test tube, to a chromatography matrix, etc., either covalently or non-covalently. Proteins can be covalently immobilized using any method well known in the art, for example, but not limited to the method of Kadonaga and Tjian, 1986, *Proc. Natl. Acad. Sci. USA* 83:5889-5893, i.e., linkage to a cyanogen-bromide derivatized substrate such as CNBr-Sepharose 4B (Pharmacia). Where needed, the use of spacers can reduce steric hindrance by the substrate. Non-covalent attachment of proteins to a substrate include, but are not limited to, attachment of a protein to a charged surface, binding with specific antibodies, binding to a third unrelated interacting protein, etc.

Assays of agents (including cell extracts or a library pool) for competition for binding of one member of a complex (or derivatives thereof) with another member of the complex labeled by any means (e.g., those means described above) are provided to screen for competitors or enhancers of complex formation.

In specific embodiments, blocking agents to inhibit non-specific binding of reagents to other protein components, or absorptive losses of reagents to plastics, immobilization matrices, etc., are included in the assay mixture. Blocking agents include, but are not restricted to bovine serum albumin, β -casein, nonfat dried milk, Denhardt's reagent, Ficoll, polyvinylpyrrolidone, nonionic detergents (NP40, Triton X-100, Tween 20, Tween 80, etc.), ionic detergents (e.g., SDS, LDS, etc.), polyethylene glycol, etc. Appropriate blocking agent concentrations allow complex formation.

After binding is performed, unbound, labeled protein is removed in the supernatant, and the immobilized protein retaining any bound, labeled protein is washed extensively. The amount of bound label is then quantified using standard methods in the art to detect the label as described, *supra*.

In another specific embodiments screening for modulators of the protein complexes/protein as provided herein can be carried out by attaching those and/or the antibodies as provided herein to a solid carrier. In a further specific embodiment, the invention relates to an array of said molecules.

The preparation of such an array containing different types of proteins, including antibodies) is well known in the art and is apparent to a person skilled in the art (see e.g. Ekins et al., 1989, *J. Pharm. Biomed. Anal.* 7:155-168; Mitchell et al. 2002, *Nature Biotechnol.* 20:225-229; Petricoin et al., 2002, *Lancet* 359:572-577; Templin et al., 2001, *Trends Biotechnol.* 20:160-166; Wilson and Nock, 2001, *Curr. Opin. Chem. Biol.* 6:81-85; Lee et al., 2002 *Science* 295:1702-1705; MacBeath and Schreiber, 2000, *Science* 289:1760; Blawas and Reichert, 1998, *Biomaterials* 19:595; Kane et al., 1999, *Biomaterials* 20:2363; Chen et al., 1997, *Science* 276:1425; Vaughan et al., 1996, *Nature Biotechnol.* 14:309-314; Mahler et al., 1997, *Immunotechnology* 3:31-43; Roberts et al., 1999, *Curr. Opin. Chem. Biol.* 3:268-273; Nord et al., 1997, *Nature Biotechnol.* 15:772-777; Nord et al., 2001, *Eur. J. Biochem.* 268:4269-4277; Brody and Gold, 2000, *Rev. Mol. Biotechnol.* 74:5-13; Karlstroem and Nygren, 2001, *Anal. Biochem.* 295:22-30; Nelson et al., 2000, *Electrophoresis* 21:1155-1163; Honore et al., 2001, *Expert Rev. Mol. Diagn.* 3:265-274; Albala, 2001, *Expert Rev. Mol. Diagn.* 2:145-152, Figeys and Pinto, 2001, *Electrophoresis* 22:208-216 and references in the publications listed here).

Complexes can be attached to an array by different means as will be apparent to a person skilled in the art. Complexes can for example be added to the array via a TAP-tag (as described in WO/0009716 and in Rigaut et al., 1999, *Nature Biotechnol.* 10:1030-1032) after the purification step or by another suitable purification scheme as will be apparent to a person skilled in the art.

Optionally, the proteins of the complex can be cross-linked to enhance the stability of the complex. Different methods to cross-link proteins are well known in the art. Reactive end-groups of cross-linking agents include but are not limited to -COOH, -SH, -NH₂ or N-oxy-succinamate.

The spacer of the cross-linking agent should be chosen with respect to the size of the complex to be cross-linked. For small protein complexes, comprising only a few proteins, relatively short spacers are preferable in order to reduce the likelihood of cross-linking separate complexes in the reaction mixture. For larger protein complexes, additional use of larger spacers is preferable in order to facilitate cross-linking between proteins within the complex.

It is preferable to check the success-rate of cross-linking before linking the complex to the carrier.

As will be apparent to a person skilled in the art, the optimal rate of cross-linking need to be determined on a case by case basis. This can be achieved by methods well known in the art, some of which are exemplary described below.

A sufficient rate of cross-linking can be checked f.e. by analysing the cross-linked complex vs. a non-cross-linked complex on a denaturing protein gel.

If cross-linking has been performed successfully, the proteins of the complex are expected to be found in the same lane, whereas the proteins of the non-cross-linked complex are expected to be separated according to their individual characteristics. Optionally the presence of all proteins of the complex can be further checked by peptide-sequencing of proteins in the respective bands using methods well known in the art such as mass spectrometry and/or Edman degradation.

In addition, a rate of crosslinking which is too high should also be avoided. If cross-linking has been carried out too extensively, there will be an increasing amount of cross-linking of the individual protein complex, which potentially interferes with a screening for potential binding partners and/or modulators etc. using the arrays.

The presence of such structures can be determined by methods well known in the art and include e.g. gel-filtration experiments comparing the gel filtration profile solutions containing cross-linked complexes vs. uncross-linked complexes.

Optionally, functional assays as will be apparent to a person skilled in the art, some of which are exemplarily provided herein, can be performed to check the integrity of the complex.

Alternatively, members of the protein complex can be expressed as a single fusion protein and coupled to the matrix as will be apparent to a person skilled in the art.

Optionally, the attachment of the complex or proteins or antibody as outlined above can be further monitored by various methods apparent to a person skilled in the art. Those include, but are not limited to surface plasmon resonance (see e.g. McDonnel, 2001, *Curr. Opin. Chem. Biol.* 5:572-577; Lee, 2001, *Trends Biotechnol.* 19:217-222; Weinberger et al., 2000, 1:395-416; Pearson et al., 2000, *Ann. Clin. Biochem.* 37:119-145; Vely et al., 2000, *Methods Mol. Biol.* 121:313-321; Slepak, 2000, *J. Mol. Recognit.* 13:20-26.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Presenilin 1 complex, Presenilin 2 complex, Nicastrin complex, Aph-1a complex, Aph-1b complex, Pen-2 complex, BACE1 D215N complex, APP complex, APP695SW complex, APP-C99 complex, X11beta complex, Fe65 complex, include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the gamma-secretase activity in vitro of the Presenilin 1 complex include but are not limited to those described in Li Y M et al., 2000, Proc Natl Acad Sci U S A, 97:6138-43 and Pinnix I et al., 2001, J Biol Chem, 276:481-7.

Exemplary assays useful for measuring the gamma-secretase dependent transcriptional activity of the Presenilin 1 complex include but are not limited to those described in Karlstrom H et al., 2002, J Biol Chem, 277:6763-6.

Exemplary assays useful for measuring the formation of amyloid-beta peptides and their aggregated forms of the Presenilin 1 complex include but are not limited to those described in De Strooper B et al., 1998, Nature, 391:387-90.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Presenilin 1 complex, Presenilin 2 complex, Nicastrin complex, Aph-1a complex, Aph-1b complex, Pen-2 complex, BACE1 D215N complex, APP complex, APP695SW complex, APP-C99 complex, X11beta complex, Fe65 complex, include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Presenilin 1 complex, Presenilin 2 complex, Nicastrin complex, Aph-1a complex, Aph-1b complex, Pen-2 complex, BACE1 D215N complex, APP complex, APP695SW complex, APP-C99 complex, X11beta complex, Fe65 complex, include but are not limited to those described in Tian G et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Presenilin 1 complex, Presenilin 2 complex, Nicastrin complex, Aph-1a complex, Aph-1b complex, Pen-2 complex, BACE1 D215N complex, APP complex, APP695SW complex, APP-C99 complex, Fe65 complex, include but are not limited to those described in Cao X et al., 2001, *Science*, 293:115-20.

Exemplary assays useful for measuring the phosphorylation of Tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau complex include but are not limited to those described in Drewes G et al., 1997, *Cell*, 89:297-308.

Exemplary assays useful for measuring the aggregation of Tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau complex include but are not limited to those described in Barghorn S et al., 2000, *Biochemistry*, 39:11714-21.

Exemplary assays useful for measuring the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11beta complex include but are not limited to those described in Biederer T et al., 2002, *J Neurosci*, 22:7340-51.

Exemplary assays useful for measuring the activation of Calsenilin target genes including prodynorphin that contain DRE elements (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Calsenilin complex include but are not limited to those described in Cheng Hai-Ying M et al., 2002, *Cell*, 108:31-43.

Exemplary assays useful for measuring the activation or inactivation of potassium channels by compounds (e.g. Retigabine) and their effect on transcriptional processes regulated directly or indirectly by Calsenilin of the Calsenilin complex include but are not limited to those described in Rundfeldt C et al., 1997, *Eur J Pharmacol*, 336:243-9.

4.6.1 CANDIDATE MOLECULES

Any molecule known in the art can be tested for its ability to modulate (increase or decrease) the amount of, activity of, or protein component composition of a complex of the present invention as detected by a change in the amount of, activity of, or protein component composition of, said complex. By way of example, a change in the amount of the complex can be detected by detecting a change in the amount of the complex that can be isolated from a cell expressing the complex machinery. For identifying a molecule that modulates complex activity, candidate molecules can be directly provided to a cell expressing the complex machinery, or, in the case of candidate proteins, can be provided by providing their encoding nucleic acids under conditions in which the nucleic acids are recombinantly expressed to produce the candidate proteins within the cell expressing the complex machinery, the complex is then isolated from the cell and the isolated complex is assayed for activity using methods well known in the art, not limited to those described, *supra*.

This embodiment of the invention is well suited to screen chemical libraries for molecules which modulate, e.g., inhibit, antagonize, or agonize, the amount of, activity of, or protein component composition of the complex. The chemical libraries can be peptide libraries, peptidomimetic libraries, chemically synthesized libraries, recombinant, e.g., phage display libraries, and in vitro translation-based libraries, other non-peptide synthetic organic libraries, etc.

Exemplary libraries are commercially available from several sources (ArQule, Tripos/PanLabs, ChemDesign, Pharmacopoeia). In some cases, these chemical libraries are generated using combinatorial strategies that encode the identity of each member of the library on a substrate to which the member compound is attached, thus allowing direct and immediate identification of a molecule that is an effective modulator. Thus, in many combinatorial approaches, the position on a plate of a compound specifies that compound's composition. Also, in one example, a single plate position may have from 1-20 chemicals that can be screened by administration to a well containing the interactions of interest. Thus, if modulation is detected, smaller and smaller pools of interacting pairs can be assayed for the modulation activity. By such methods, many candidate molecules can be screened.

Many diversity libraries suitable for use are known in the art and can be used to provide compounds to be tested according to the present invention. Alternatively, libraries can be constructed using standard methods. Chemical (synthetic) libraries,

recombinant expression libraries, or polysome-based libraries are exemplary types of libraries that can be used.

The libraries can be constrained or semirigid (having some degree of structural rigidity), or linear or nonconstrained. The library can be a cDNA or genomic expression library, random peptide expression library or a chemically synthesized random peptide library, or non-peptide library. Expression libraries are introduced into the cells in which the assay occurs, where the nucleic acids of the library are expressed to produce their encoded proteins.

In one embodiment, peptide libraries that can be used in the present invention may be libraries that are chemically synthesized in vitro. Examples of such libraries are given in Houghten et al., 1991, *Nature* 354:84-86, which describes mixtures of free hexapeptides in which the first and second residues in each peptide were individually and specifically defined; Lam et al., 1991, *Nature* 354:82-84, which describes a "one bead, one peptide" approach in which a solid phase split synthesis scheme produced a library of peptides in which each bead in the collection had immobilized thereon a single, random sequence of amino acid residues; Medynski, 1994, *Bio/Technology* 12:709-710, which describes split synthesis and T-bag synthesis methods; and Gallop et al., 1994, *J. Med. Chem.* 37:1233-1251. Simply by way of other examples, a combinatorial library may be prepared for use, according to the methods of Ohlmeyer et al., 1993, *Proc. Natl. Acad. Sci. USA* 90:10922-10926; Erb et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:11422-11426; Houghten et al., 1992, *Biotechniques* 13:412; Jayawickreme et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:1614-1618; or Salmon et al., 1993, *Proc. Natl. Acad. Sci. USA* 90:11708-11712. PCT Publication No. WO 93/20242 and Brenner and Lerner, 1992, *Proc. Natl. Acad. Sci. USA* 89:5381-5383 describe "encoded combinatorial chemical libraries," that contain oligonucleotide identifiers for each chemical polymer library member.

In a preferred embodiment, the library screened is a biological expression library that is a random peptide phage display library, where the random peptides are constrained (e.g., by virtue of having disulfide bonding).

Further, more general, structurally constrained, organic diversity (e.g., nonpeptide) libraries, can also be used. By way of example, a benzodiazepine library (see e.g., Bunin et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:4708-4712) may be used.

Conformationally constrained libraries that can be used include but are not limited to those containing invariant cysteine residues which, in an oxidizing environment, cross-

link by disulfide bonds to form cystines, modified peptides (e.g., incorporating fluorine, metals, isotopic labels, are phosphorylated, etc.), peptides containing one or more non-naturally occurring amino acids, non-peptide structures, and peptides containing a significant fraction of γ -carboxyglutamic acid.

Libraries of non-peptides, e.g., peptide derivatives (for example, that contain one or more non-naturally occurring amino acids) can also be used. One example of these are peptoid libraries (Simon et al., 1992, Proc. Natl. Acad. Sci. USA 89:9367-9371). Peptoids are polymers of non-natural amino acids that have naturally occurring side chains attached not to the α carbon but to the backbone amino nitrogen. Since peptoids are not easily degraded by human digestive enzymes, they are advantageously more easily adaptable to drug use. Another example of a library that can be used, in which the amide functionalities in peptides have been permethylated to generate a chemically transformed combinatorial library, is described by Ostresh et al., 1994, Proc. Natl. Acad. Sci. USA 91:11138-11142).

The members of the peptide libraries that can be screened according to the invention are not limited to containing the 20 naturally occurring amino acids. In particular, chemically synthesized libraries and polysome based libraries allow the use of amino acids in addition to the 20 naturally occurring amino acids (by their inclusion in the precursor pool of amino acids used in library production). In specific embodiments, the library members contain one or more non-natural or non-classical amino acids or cyclic peptides. Non-classical amino acids include but are not limited to the D-isomers of the common amino acids, γ -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid; γ -Abu, γ -Ahx, 6-amino hexanoic acid; Aib, 2-amino isobutyric acid; 3-amino propionic acid; ornithine; norleucine; norvaline, hydroxyproline, sarcosine, citrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, β -alanine, designer amino acids such as β -methyl amino acids, γ -methyl amino acids, N-methyl amino acids, fluoro-amino acids and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

In a specific embodiment, fragments and/or analogs of complexes of the invention, or protein components thereof, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex activity or formation.

In another embodiment of the present invention, combinatorial chemistry can be used to identify modulators of the complexes. Combinatorial chemistry is capable of creating libraries containing hundreds of thousands of compounds, many of which may

be structurally similar. While high throughput screening programs are capable of screening these vast libraries for affinity for known targets, new approaches have been developed that achieve libraries of smaller dimension but which provide maximum chemical diversity. (See e.g., Matter, 1997, *J. Med. Chem.* 40:1219-1229).

One method of combinatorial chemistry, affinity fingerprinting, has previously been used to test a discrete library of small molecules for binding affinities for a defined panel of proteins. The fingerprints obtained by the screen are used to predict the affinity of the individual library members for other proteins or receptors of interest (in the instant invention, the protein complexes of the present invention and protein components thereof.) The fingerprints are compared with fingerprints obtained from other compounds known to react with the protein of interest to predict whether the library compound might similarly react. For example, rather than testing every ligand in a large library for interaction with a complex or protein component, only those ligands having a fingerprint similar to other compounds known to have that activity could be tested. (See, e.g., Kauvar et al., 1995, *Chem. Biol.* 2:107-118; Kauvar, 1995, *Affinity fingerprinting*, Pharmaceutical Manufacturing International. 8:25-28; and Kauvar, *Toxic-Chemical Detection by Pattern Recognition in New Frontiers in Agrochemical Immunoassay*, Kurtz, Stanker and Skerritt (eds), 1995, AOAC: Washington, D.C., 305-312).

Kay et al. (1993, *Gene* 128:59-65) disclosed a method of constructing peptide libraries that encode peptides of totally random sequence that are longer than those of any prior conventional libraries. The libraries disclosed in Kay et al. encode totally synthetic random peptides of greater than about 20 amino acids in length. Such libraries can be advantageously screened to identify complex modulators. (See also U.S. Patent No. 5,498,538 dated March 12, 1996; and PCT Publication No. WO 94/18318 dated August 18, 1994).

A comprehensive review of various types of peptide libraries can be found in Gallop et al., 1994, *J. Med. Chem.* 37:1233-1251.

4.7 PHARMACEUTICAL COMPOSITIONS AND THERAPEUTIC/PROPHYLACTIC ADMINISTRATION

The invention provides methods of treatment (and prophylaxis) by administration to a subject of an effective amount of a therapeutic of the invention. In a preferred

aspect, the therapeutic is substantially purified. The subject is preferably an animal including, but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human. In a specific embodiment, a non-human mammal is the subject.

Various delivery systems are known and can be used to administer a therapeutic of the invention, e.g., encapsulation in liposomes, microparticles, and microcapsules; use of recombinant cells capable of expressing the therapeutic, use of receptor-mediated endocytosis (e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432); construction of a therapeutic nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion, by bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral, rectal and intestinal mucosa, etc.), and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment. This may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) of a malignant tumor or neoplastic or pre-neoplastic tissue.

In another embodiment, the therapeutic can be delivered in a vesicle, in particular a liposome (Langer, 1990, *Science* 249:1527-1533; Treat et al., 1989, In: *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler, eds., Liss, New York, pp. 353-365; Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

In yet another embodiment, the therapeutic can be delivered via a controlled release system. In one embodiment, a pump may be used (Langer, *supra*; Sefton, 1987, CRC Crit. Ref. Biomed. Eng. 14:201-240; Buchwald et al., 1980, Surgery 88:507-516; Saudek et al., 1989, N. Engl. J. Med. 321:574-579). In another embodiment, polymeric materials can be used (Medical Applications of Controlled Release, Langer and Wise, eds., CRC Press, Boca Raton, Florida, 1974; Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball, eds., Wiley, New York, 1984; Ranger and Peppas, 1983, Macromol. Sci. Rev. Macromol. Chem. 23:61; Levy et al., 1985, Science 228:190-192; During et al., 1989, Ann. Neurol. 25:351-356; Howard et al., 1989, J. Neurosurg. 71:858-863). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (e.g., Goodson, 1984, In: Medical Applications of Controlled Release, *supra*, Vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer (1990, Science 249:1527-1533).

In a specific embodiment where the therapeutic is a nucleic acid encoding a protein therapeutic, the nucleic acid can be administered *in vivo* to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or by coating it with lipids, cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (e.g., Joliot et al., 1991, Proc. Natl. Acad. Sci. USA 88:1864-1868), etc. Alternatively, a nucleic acid therapeutic can be introduced intracellularly and incorporated by homologous recombination within host cell DNA for expression.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a therapeutic, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly, in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not

limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated, in accordance with routine procedures, as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water or saline for injection can be provided so that the ingredients may be mixed prior to administration.

The therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free carboxyl groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., those formed with free amine groups such as those derived from isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc., and those derived from sodium, potassium, ammonium, calcium, and ferric hydroxides, etc.

The amount of the therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20-500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. For example, the kit can comprise in one or more containers a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins listed in the third column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fourth column of table 1.

Alternatively, the kit can comprise in one or more containers, all proteins, functionally active fragments or functionally active derivatives thereof of from the group of proteins in the fifth column of table 1.

The kits of the present invention can also contain expression vectors encoding the essential components of the complex machinery, which components after being expressed can be reconstituted in order to form a biologically active complex. Such a kit preferably also contains the required buffers and reagents. Optionally associated with such container(s) can be instructions for use of the kit and/or a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

4.8 ANIMAL MODELS

The present invention also provides animal models. In one embodiment, animal models for diseases and disorders involving the protein complexes of the present invention are provided. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention. Such animals can be initially produced by promoting homologous recombination or insertional mutagenesis between genes encoding the protein components of the complexes in the chromosome, and exogenous genes encoding the protein components of the complexes that have been rendered biologically inactive or deleted (preferably by insertion of a heterologous sequence, e.g., an antibiotic resistance gene). In a preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which a gene encoding a component protein from the third column of table 1, or a functionally active fragment or functionally active derivative thereof, and a gene encoding a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, has been inactivated or deleted (Capecchi, 1989, Science 244:1288-1292).

In another preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which the genes of all component proteins from the group of proteins listed in the third column of table 1 or of all proteins from the group of proteins listed in the forth column of table 1 have been inactivated or deleted.

The chimeric animal can be bred to produce additional knockout animals. Such animals can be mice, hamsters, sheep, pigs, cattle, etc., and are preferably non-human mammals. In a specific embodiment, a knockout mouse is produced.

Such knockout animals are expected to develop, or be predisposed to developing, diseases or disorders associated with mutations involving the protein complexes of the present invention, and thus, can have use as animal models of such diseases and disorders, e.g., to screen for or test molecules (e.g., potential therapeutics) for such diseases and disorders.

In a different embodiment of the invention, transgenic animals that have incorporated and express (or over-express or mis-express) a functional gene encoding a protein component of the complex, e.g. by introducing the a gene encoding one or more of the components of the complex under the control of a heterologous promoter (i.e., a promoter that is not the native promoter of the gene) that either over-expresses the protein or proteins, or expresses them in tissues not normally expressing the complexes or proteins, can have use as animal models of diseases and disorders characterized by elevated levels of the protein complexes. Such animals can be used to screen or test molecules for the ability to treat or prevent the diseases and disorders cited supra.

In one embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group of proteins listed in the third column of table 1, and an endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fourth column of table 1 has been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof. In addition, the present invention provides a recombinant non-human animal in which the

endogenous genes of all proteins, or functionally active fragments or functionally active derivatives thereof of one of the group of proteins listed in the fifth column have been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof:

In another embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins of the third column of table 1, and endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins of the fourth column, of table 1 are recombinantly expressed in said animal or an ancestor thereof.

The following series of examples are presented by way of illustration and not by way of limitation on the scope of the invention.

EXAMPLES

An object of the present invention was to identify protein complexes of the APP processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Those complexes are, as called herein, the following complexes: Presenilin 1 complex, Presenilin 2 complex, Nicastrin complex, Aph-1a complex, Aph-1b complex, Pen-2 complex, BACE1 N215D complex, APP complex, APP695SW complex, APP-C99 complex, Tau complex, X11beta complex, Fe65 complex and Calsenilin complex.

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

Thus the invention relates to the Presenilin 1 complex:

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "Alpha catenin" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha catenin" encoded by a nucleic acid that hybridizes to the "Alpha catenin" nucleic acid or its complement under low stringency conditions,

(ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(iii) "Beta catenin" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta catenin" encoded by a nucleic acid that hybridizes to the "Beta catenin" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(v) "Delta-2 catenin" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-2 catenin" encoded by a nucleic acid that hybridizes to the "Delta-2 catenin" nucleic acid or its complement under low stringency conditions,

(vi) "Gamma catenin" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Gamma catenin" encoded by a nucleic acid that hybridizes to the "Gamma catenin" nucleic acid or its complement under low stringency conditions,

(vii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (viii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (ix) "Plakophilin 4" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Plakophilin 4" encoded by a nucleic acid that hybridizes to the "Plakophilin 4" nucleic acid or its complement under low stringency conditions,
- (x) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and
- (xi) "Ubiquilin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquilin" encoded by a nucleic acid that hybridizes to the "Ubiquilin" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "BAX inhibitor 1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BAX inhibitor 1" encoded by a nucleic acid that hybridizes to the "BAX inhibitor 1" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions,
- (iii) "Cadherin-11 precursor" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-11 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-11 precursor" nucleic acid or its complement under low stringency conditions,
- (iv) "Cadherin-4 precursor" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-4 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-4 precursor" nucleic acid or its complement under low stringency conditions,

(v) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions,

(vi) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions,

(vii) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(viii) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and

(ix) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. The protein complex according to No. 1 wherein the first protein is the protein "Presenilin 1" (SEQ ID No:17), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "Alpha catenin" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha catenin" encoded by a nucleic acid that hybridizes to the "Alpha catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (iii) "BAX inhibitor 1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BAX inhibitor 1" encoded by a nucleic acid that hybridizes to the "BAX inhibitor 1" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta catenin" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta catenin" encoded by a nucleic acid that hybridizes to the "Beta catenin" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions,
- (vi) "Cadherin-11 precursor" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-11 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-11 precursor" nucleic acid or its complement under low stringency conditions,
- (vii) "Cadherin-4 precursor" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-4 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-4 precursor" nucleic acid or its complement under low stringency conditions,
- (viii) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

- (ix) "Delta-2 catenin" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-2 catenin" encoded by a nucleic acid that hybridizes to the "Delta-2 catenin" nucleic acid or its complement under low stringency conditions,
- (x) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions,
- (xi) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions,
- (xii) "Gamma catenin" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Gamma catenin" encoded by a nucleic acid that hybridizes to the "Gamma catenin" nucleic acid or its complement under low stringency conditions,
- (xiii) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xiv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xvi) "Plakophilin 4" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Plakophilin 4" encoded by a nucleic acid that hybridizes to the "Plakophilin 4" nucleic acid or its complement under low stringency conditions,
- (xvii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1"

encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xviii) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(xix) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Ubiquilin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquilin" encoded by a nucleic acid that hybridizes to the "Ubiquilin" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 8 of the following proteins:

(i) "Alpha catenin" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha catenin" encoded by a nucleic acid that hybridizes to the "Alpha catenin" nucleic acid or its complement under low stringency conditions,

(ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(iii) "BAX inhibitor 1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BAX inhibitor 1" encoded by a nucleic acid that hybridizes to the "BAX inhibitor 1" nucleic acid or its complement under low stringency conditions,

(iv) "Beta catenin" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta catenin" encoded by a nucleic acid that hybridizes to the "Beta catenin" nucleic acid or its complement under low stringency conditions,

- (v) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions,
- (vi) "Cadherin-11 precursor" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-11 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-11 precursor" nucleic acid or its complement under low stringency conditions,
- (vii) "Cadherin-4 precursor" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-4 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-4 precursor" nucleic acid or its complement under low stringency conditions,
- (viii) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (ix) "Delta-2 catenin" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-2 catenin" encoded by a nucleic acid that hybridizes to the "Delta-2 catenin" nucleic acid or its complement under low stringency conditions,
- (x) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions,
- (xi) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions,
- (xii) "Gamma catenin" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Gamma catenin" encoded by a nucleic acid that hybridizes to the "Gamma catenin" nucleic acid or its complement under low stringency conditions,
- (xiii) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442"

encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xiv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xvi) "Plakophilin 4" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Plakophilin 4" encoded by a nucleic acid that hybridizes to the "Plakophilin 4" nucleic acid or its complement under low stringency conditions,

(xvii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xviii) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(xix) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xx) "Ubiquilin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquilin" encoded by a nucleic acid that hybridizes to the "Ubiquilin" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the

functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), gamma -secretase activity in vitro, gamma -secretase activity in vitro, gamma -secretase dependent transcriptional activity, formation of amyloid-beta peptides and their aggregated forms, the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Presenilin 1 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Presenilin 1 complex selected from:

- (i) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions,
- (ii) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions,
- (iv) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and
- (v) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA,

and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

(a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions,

(ii) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions,

(iii) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions,

(iv) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(v) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a

nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions,

(ii) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions,

(iii) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions,

(iv) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(v) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, comprising the steps of:

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing Presenilin 1 complex to one or more candidate molecules; and
 - (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether (i) "Alpha catenin" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha

catenin" encoded by a nucleic acid that hybridizes to the "Alpha catenin" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(iii) "BAX inhibitor 1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BAX inhibitor 1" encoded by a nucleic acid that hybridizes to the "BAX inhibitor 1" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Beta catenin" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta catenin" encoded by a nucleic acid that hybridizes to the "Beta catenin" nucleic acid or its complement under low stringency conditions, and/or

(v) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Cadherin-11 precursor" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-11 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-11 precursor" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Cadherin-4 precursor" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-4 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-4 precursor" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Delta-2 catenin" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-2 catenin" encoded by a nucleic acid that hybridizes to the "Delta-2 catenin" nucleic acid or its complement under low stringency conditions, and/or

- (x) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Gamma catenin" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Gamma catenin" encoded by a nucleic acid that hybridizes to the "Gamma catenin" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Plakophilin 4" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Plakophilin 4" encoded by a nucleic acid that hybridizes to the "Plakophilin 4" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1"

encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Ubiquilin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquilin" encoded by a nucleic acid that hybridizes to the "Ubiquilin" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a

comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "Alpha catenin" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha catenin" encoded by a nucleic acid that hybridizes to the "Alpha catenin" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "BAX inhibitor 1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BAX inhibitor 1" encoded by a nucleic acid that hybridizes to the "BAX inhibitor 1" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Beta catenin" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta

catenin" encoded by a nucleic acid that hybridizes to the "Beta catenin" nucleic acid or its complement under low stringency conditions, and/or

(v) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Cadherin-11 precursor" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-11 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-11 precursor" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Cadherin-4 precursor" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-4 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-4 precursor" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Delta-2 catenin" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-2 catenin" encoded by a nucleic acid that hybridizes to the "Delta-2 catenin" nucleic acid or its complement under low stringency conditions, and/or

(x) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions, and/or

(xi) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Gamma catenin" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Gamma catenin" encoded by a nucleic acid that hybridizes to the "Gamma catenin" nucleic acid or its complement under low stringency conditions, and/or

- (xiii) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Plakophilin 4" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Plakophilin 4" encoded by a nucleic acid that hybridizes to the "Plakophilin 4" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Ubiquilin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquilin" encoded by a nucleic acid that hybridizes to the "Ubiquilin" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), gamma -secretase activity in vitro, gamma -secretase activity in vitro, gamma -secretase dependent transcriptional activity, formation of amyloid-beta peptides and their aggregated forms, the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:
(i) "Alpha catenin" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha

catenin" encoded by a nucleic acid that hybridizes to the "Alpha catenin" nucleic acid or its complement under low stringency conditions,

(ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(iii) "BAX inhibitor 1" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BAX inhibitor 1" encoded by a nucleic acid that hybridizes to the "BAX inhibitor 1" nucleic acid or its complement under low stringency conditions,

(iv) "Beta catenin" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta catenin" encoded by a nucleic acid that hybridizes to the "Beta catenin" nucleic acid or its complement under low stringency conditions,

(v) "CGI-147" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-147" encoded by a nucleic acid that hybridizes to the "CGI-147" nucleic acid or its complement under low stringency conditions,

(vi) "Cadherin-11 precursor" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-11 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-11 precursor" nucleic acid or its complement under low stringency conditions,

(vii) "Cadherin-4 precursor" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin-4 precursor" encoded by a nucleic acid that hybridizes to the "Cadherin-4 precursor" nucleic acid or its complement under low stringency conditions,

(viii) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(ix) "Delta-2 catenin" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-2 catenin" encoded by a nucleic acid that hybridizes to the "Delta-2 catenin" nucleic acid or its complement under low stringency conditions,

- (x) "FKRP" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FKRP" encoded by a nucleic acid that hybridizes to the "FKRP" nucleic acid or its complement under low stringency conditions,
- (xi) "FLJ20627" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20627" encoded by a nucleic acid that hybridizes to the "FLJ20627" nucleic acid or its complement under low stringency conditions,
- (xii) "Gamma catenin" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Gamma catenin" encoded by a nucleic acid that hybridizes to the "Gamma catenin" nucleic acid or its complement under low stringency conditions,
- (xiii) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xiv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xvi) "Plakophilin 4" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Plakophilin 4" encoded by a nucleic acid that hybridizes to the "Plakophilin 4" nucleic acid or its complement under low stringency conditions,
- (xvii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xviii) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1"

encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(xix) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or(xx) "Ubiquilin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquilin" encoded by a nucleic acid that hybridizes to the "Ubiquilin" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the Fe65 complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
 - (ii) "APLP2" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
 - (iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
 - (iv) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99"

encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "RNB6" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and

(vii) "Transcription factor CP2 " (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Transcription factor CP2 " encoded by a nucleic acid that hybridizes to the "Transcription factor CP2 " nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "14-3-3 protein epsilon" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,

(ii) "14-3-3 protein beta/alpha" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,

(iii) "14-3-3 protein eta" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,

(iv) "14-3-3 protein gamma" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,

- (v) "14-3-3 protein tau" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (viii) "ECP-51" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (ix) "GAP-associated tyrosine phosphoprotein p62 " (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62 " encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62 " nucleic acid or its complement under low stringency conditions,
- (x) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,
- (xi) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (xii) "PDZ domain protein MAGI-3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, (xiii) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiv) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions,

(xv) "SAP-62" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and

(xvi) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

2. The protein complex according to No. 1 wherein the first protein is the protein "Fe65" (SEQ ID No:33), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (ix) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62 " (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62 " encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62 " nucleic acid or its complement under low stringency conditions,
- (xv) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,
- (xvi) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that

hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xvii) "PDZ domain protein MAGI-3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xviii) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xix) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions,

(xx) "RNB6" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxi) "SAP-62" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxii) "Transcription factor CP2 " (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Transcription factor CP2 " encoded by a nucleic acid that hybridizes to the "Transcription factor CP2 " nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc

finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 15 of the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

- (viii) "APLP2" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ix) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62 " (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62 " encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62 " nucleic acid or its complement under low stringency conditions,
- (xv) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,

(xvi) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xvii) "PDZ domain protein MAGI-3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xviii) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xix) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions,

(xx) "RNB6" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxi) "SAP-62" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxii) "Transcription factor CP2 " (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Transcription factor CP2 " encoded by a nucleic acid that hybridizes to the

"Transcription factor CP2 " nucleic acid or its complement under low stringency conditions,

(xxiii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Fe65 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Fe65 complex selected from:

- (i) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (ii) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions, and
- (iii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at

40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
- (i) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
 - (ii) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following proteins:

- (i) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (ii) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

- (a) exposing said complex, or a cell or organism containing Fe65 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether
(i) "14-3-3 protein epsilon" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or
(ii) "14-3-3 protein beta/alpha" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or

- (iii) "14-3-3 protein eta" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "14-3-3 protein gamma" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or
- (v) "14-3-3 protein tau" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "APLP2" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (x) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue

- thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "ECP-51" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "GAP-associated tyrosine phosphoprotein p62 " (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62 " encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62 " nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "PDZ domain protein MAGI-3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B,

alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions, and/or

(xx) "RNB6" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "SAP-62" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Transcription factor CP2 " (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Transcription factor CP2 " encoded by a nucleic acid that hybridizes to the "Transcription factor CP2 " nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the

candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "14-3-3 protein epsilon" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "14-3-3 protein eta" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "14-3-3 protein gamma" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or
- (v) "14-3-3 protein tau" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a

nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(viii) "APLP2" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

(ix) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(x) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or

(xii) "ECP-51" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "GAP-associated tyrosine phosphoprotein p62 " (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62 " encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62 " nucleic acid or its complement under low stringency conditions, and/or

(xv) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "PDZ domain protein MAGI-3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions, and/or

(xx) "RNB6" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "SAP-62" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Transcription factor CP2 " (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Transcription factor CP2 " encoded by a nucleic acid that hybridizes to the "Transcription factor CP2 " nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a

nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(viii) "APLP2" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(ix) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(x) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,

(xii) "ECP-51" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,

(xiii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(xiv) "GAP-associated tyrosine phosphoprotein p62 " (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62 " encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62 " nucleic acid or its complement under low stringency conditions,

(xv) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

- variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,
- (xvi) "Krab box protein ensp00000302970" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (xvii) "PDZ domain protein MAGI-3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,
- (xviii) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,
- (xix) "Protein similar to probable mitotic centromere associated kinesin " (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin " encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin " nucleic acid or its complement under low stringency conditions,
- (xx) "RNB6" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,
- (xxi) "SAP-62" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,
- (xxii) "Transcription factor CP2 " (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Transcription factor CP2 " encoded by a nucleic acid that hybridizes to the "Transcription factor CP2 " nucleic acid or its complement under low stringency conditions, and/or (xxiii) "Zinc finger protein 277" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.

The invention further relates to the X11beta complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
 - (ii) "Munc18-1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Munc18-1" encoded by a nucleic acid that hybridizes to the "Munc18-1" nucleic acid or its complement under low stringency conditions,
 - (iii) "Neurexin-1" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
 - (iv) "Syntaxin-1" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Syntaxin-1" encoded by a nucleic acid that hybridizes to the "Syntaxin-1" nucleic acid or its complement under low stringency conditions, and

- (v) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
 - (ii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
 - (iii) "Axonemal dynein heavy chain 8" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
 - (iv) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions,
 - (v) "Calsyntenin-1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
 - (vi) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
 - (vii) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-

3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(viii) "Chondroitin sulfate proteoglycan 6 " (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chondroitin sulfate proteoglycan 6 " encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6 " nucleic acid or its complement under low stringency conditions,

(ix) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,

(x) "DC6 protein" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,

(xi) "Dynein light chain 2A " (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xii) "Dynein light chain-A " (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain-A " encoded by a nucleic acid that hybridizes to the "Dynein light chain-A " nucleic acid or its complement under low stringency conditions,

(xiii) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xiv) "Eukaryotic translation initiation factor 4A, isoform " (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform " encoded by a

nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform " nucleic acid or its complement under low stringency conditions,

(xv) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xvi) "FRAP1" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xvii) "GTP-binding protein ERA" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xviii) "HDAC2" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xix) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xx) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxi) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxii) "IKAP" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxiii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA0325" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0325" encoded by a nucleic acid that hybridizes to the "KIAA0325" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xxviii) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxix) "LIB (leucine-rich repeat protein)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xxx) "Laminin, gamma 1 " (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xxxi) "MBIP" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xxxii) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Myosin IXB" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xxxiv) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxxv) "NIPSNAP2" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

- (xxxix) "Peroxiredoxin 4" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Peroxiredoxin 4" encoded by a nucleic acid that hybridizes to the "Peroxiredoxin 4" nucleic acid or its complement under low stringency conditions,
- (xl) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,
- (xli) "Procollagen C-endopeptidase enhancer " (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Procollagen C-endopeptidase enhancer " encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer " nucleic acid or its complement under low stringency conditions,
- (xlii) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,
- (xlili) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions,
- (xliv) "RPGR-interacting protein 1" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,
- (xlv) "Reelin" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (xlii) "Serine/threonine protein phosphatase 6 " (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "Serine/threonine protein phosphatase 6 " encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6 " nucleic acid or its complement under low stringency conditions,

(xlvi) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(xlvii) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(xlviii) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions,

(i) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and

(ii) "Zinc finger protein 198 " (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 198 " encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198 " nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

2. The protein complex according to No. 1 wherein the first protein is the protein "X11beta" (SEQ ID No:96), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (v) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions,
- (vi) "Calsyntenin-1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

- (vii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (viii) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (ix) "Chondroitin sulfate proteoglycan 6 " (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chondroitin sulfate proteoglycan 6 " encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6 " nucleic acid or its complement under low stringency conditions,
- (x) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xi) "DC6 protein" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "Dynein light chain 2A " (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,
- (xiii) "Dynein light chain-A " (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain-A " encoded by a nucleic acid that hybridizes to the "Dynein light chain-A " nucleic acid or its complement under low stringency conditions,
- (xiv) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)"

encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xv) "Eukaryotic translation initiation factor 4A, isoform " (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform " encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform " nucleic acid or its complement under low stringency conditions,

(xvi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xvii) "FRAP1" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xviii) "GTP-binding protein ERA" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xix) "HDAC2" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xx) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxi) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxii) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245"

encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxiii) "IKAP" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA0325" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0325" encoded by a nucleic acid that hybridizes to the "KIAA0325" nucleic acid or its complement under low stringency conditions,

(xxviii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxx) "LIB (leucine-rich repeat protein)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to

the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Laminin, gamma 1 " (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xxxii) "MBIP" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xxxiii) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Munc18-1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Munc18-1" encoded by a nucleic acid that hybridizes to the "Munc18-1" nucleic acid or its complement under low stringency conditions,

(xxxv) "Myosin IXB" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xxxvi) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "NIPSNAP2" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Neurexin-1" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,

(xxxix) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xl) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xli) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xlii) "Peroxisredoxin 4" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Peroxisredoxin 4" encoded by a nucleic acid that hybridizes to the "Peroxisredoxin 4" nucleic acid or its complement under low stringency conditions,

(xliii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(xliv) "Procollagen C-endopeptidase enhancer " (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Procollagen C-endopeptidase enhancer " encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer " nucleic acid or its complement under low stringency conditions,

(xlv) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

- (xlv) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions,
- (xlvii) "RPGR-interacting protein 1" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,
- (xlviii) "Reelin" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (xlix) "Serine/threonine protein phosphatase 6 " (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6 " encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6 " nucleic acid or its complement under low stringency conditions,
- (l) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,
- (li) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,
- (lii) "Syntaxin-1" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Syntaxin-1" encoded by a nucleic acid that hybridizes to the "Syntaxin-1" nucleic acid or its complement under low stringency conditions,
- (liii) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions,

(liv) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(lvi) "Zinc finger protein 198 " (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 198 " encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198 " nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 50 of the following proteins:

(i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

(ii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,

- (v) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions,
- (vi) "Calsyntenin-1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (vii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (viii) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (ix) "Chondroitin sulfate proteoglycan 6 " (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chondroitin sulfate proteoglycan 6 " encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6 " nucleic acid or its complement under low stringency conditions,
- (x) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xi) "DC6 protein" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "Dynein light chain 2A " (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein

light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xiii) "Dynein light chain-A " (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain-A " encoded by a nucleic acid that hybridizes to the "Dynein light chain-A " nucleic acid or its complement under low stringency conditions,

(xiv) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xv) "Eukaryotic translation initiation factor 4A, isoform " (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform " encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform " nucleic acid or its complement under low stringency conditions,

(xvi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xvii) "FRAP1" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xviii) "GTP-binding protein ERA" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xix) "HDAC2" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xx) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2

protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxi) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxii) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxiii) "IKAP" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA0325" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0325" encoded by a nucleic acid that hybridizes to the "KIAA0325" nucleic acid or its complement under low stringency conditions,

(xxviii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564"

encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxx) "LIB (leucine-rich repeat protein)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Laminin, gamma 1 " (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xxxii) "MBIP" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xxxiii) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Munc18-1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Munc18-1" encoded by a nucleic acid that hybridizes to the "Munc18-1" nucleic acid or its complement under low stringency conditions,

(xxxv) "Myosin IXB" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xxxvi) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1"

encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "NIPSNAP2" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Neurexin-1" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,

(xxxix) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xl) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xli) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xlii) "Peroxiredoxin 4" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Peroxiredoxin 4" encoded by a nucleic acid that hybridizes to the "Peroxiredoxin 4" nucleic acid or its complement under low stringency conditions,

(xliii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(xlv) "Procollagen C-endopeptidase enhancer " (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Procollagen C-endopeptidase enhancer " encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer " nucleic acid or its complement under low stringency conditions,

(xlv) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xlvi) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions,

(xlvii) "RPGR-interacting protein 1" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,

(xlviii) "Reelin" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xlix) "Serine/threonine protein phosphatase 6 " (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6 " encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6 " nucleic acid or its complement under low stringency conditions,

(l) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(li) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lii) "Syntaxin-1" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Syntaxin-1" encoded by a nucleic acid that hybridizes to the "Syntaxin-1" nucleic acid or its complement under low stringency conditions,

(liii) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions,

(liv) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lvi) "Zinc finger protein 198 " (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 198 " encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198 " nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:
expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the X11beta complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the X11beta complex selected from

- (i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions,
- (iii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (iv) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (v) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (vii) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (viii) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

- (ix) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,
- (xi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,
- (xii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xiii) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xiv) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions,
- (xv) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (xvi) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xvii) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xviii) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xix) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions, and

(xxi) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
- (i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
 - (ii) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions,
 - (iii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
 - (iv) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
 - (v) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
 - (vi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910"

encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(vii) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(viii) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(ix) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(x) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xiii) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xiv) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions,

- (xv) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (xvi) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (xvii) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (xviii) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
- (xix) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,
- (xx) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.
25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:
- (i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
 - (ii) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions,
 - (iii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
 - (iv) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
 - (v) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
 - (vi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
 - (vii) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2

- protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (viii) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (ix) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,
- (xi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,
- (xii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xiii) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xiv) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions,
- (xv) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xvi) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xvii) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xviii) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xix) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to AGCP6688" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions, comprising the steps of:

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

- (a) exposing said complex, or a cell or organism containing X11beta complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-

- 19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Calsyntenin-1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Chondroitin sulfate proteoglycan 6 " (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "Chondroitin sulfate proteoglycan 6 " encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6 " nucleic acid or its complement under low stringency conditions, and/or

(x) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or

(xi) "DC6 protein" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Dynein light chain 2A " (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Dynein light chain-A " (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain-A " encoded by a nucleic acid that hybridizes to the "Dynein light chain-A " nucleic acid or its complement under low stringency conditions, and/or

(xiv) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Eukaryotic translation initiation factor 4A, isoform " (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform " encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform " nucleic acid or its complement under low stringency conditions, and/or

(xvi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910"

- encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "FRAP1" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "GTP-binding protein ERA" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "HDAC2" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "IKAP" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that

hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "KIAA0325" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0325" encoded by a nucleic acid that hybridizes to the "KIAA0325" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "LIB (leucine-rich repeat protein)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Laminin, gamma 1 " (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "MBIP" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MBIP" encoded by a

nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Munc18-1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Munc18-1" encoded by a nucleic acid that hybridizes to the "Munc18-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Myosin IXB" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "NIPSNAP2" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Neurexin-1" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or

(xl) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a

nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or

(xli) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "Peroxisredoxin 4" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Peroxisredoxin 4" encoded by a nucleic acid that hybridizes to the "Peroxisredoxin 4" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "Procollagen C-endopeptidase enhancer " (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Procollagen C-endopeptidase enhancer " encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer " nucleic acid or its complement under low stringency conditions, and/or

(xlv) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "RPGR-interacting protein 1" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-

interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "Reelin" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Serine/threonine protein phosphatase 6 " (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6 " encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6 " nucleic acid or its complement under low stringency conditions, and/or

(l) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions, and/or

(li) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or

(lii) "Syntaxin-1" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Syntaxin-1" encoded by a nucleic acid that hybridizes to the "Syntaxin-1" nucleic acid or its complement under low stringency conditions, and/or

(liii) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions, and/or

(liv) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or

(iv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Zinc finger protein 198 " (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 198 " encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198 " nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a

comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or

(v) "Cadherin EGF LAG seven-pass G-type receptor 2 " (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2 " encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2 " nucleic acid or its complement under low stringency conditions, and/or

(vi) "Calsyntenin-1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Chondroitin sulfate proteoglycan 6 " (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chondroitin sulfate proteoglycan 6 " encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6 " nucleic acid or its complement under low stringency conditions, and/or

(x) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or

(xi) "DC6 protein" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DC6 protein"

encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Dynein light chain 2A " (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Dynein light chain-A " (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain-A " encoded by a nucleic acid that hybridizes to the "Dynein light chain-A " nucleic acid or its complement under low stringency conditions, and/or

(xiv) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Eukaryotic translation initiation factor 4A, isoform " (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform " encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform " nucleic acid or its complement under low stringency conditions, and/or

(xvi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "FRAP1" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "GTP-binding protein ERA" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or

(xix) "HDAC2" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or

(xx) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "IKAP" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "KIAA0325" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0325" encoded by a nucleic acid that hybridizes to the "KIAA0325" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "LIB (leucine-rich repeat protein)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Laminin, gamma 1 " (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "MBIP" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Munc18-1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Munc18-1" encoded by a nucleic acid that hybridizes to the "Munc18-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Myosin IXB" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "NIPSNAP2" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Neurexin-1" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or

(xl) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or

(xli) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "Peroxiredoxin 4" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Peroxiredoxin 4" encoded by a nucleic acid that hybridizes to the "Peroxiredoxin 4" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "Procollagen C-endopeptidase enhancer " (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Procollagen C-endopeptidase enhancer " encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer " nucleic acid or its complement under low stringency conditions, and/or

(xlv) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "RPGR-interacting protein 1" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "Reelin" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Serine/threonine protein phosphatase 6 " (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6 " encoded by a nucleic acid that

hybridizes to the "Serine/threonine protein phosphatase 6 " nucleic acid or its complement under low stringency conditions, and/or

(I) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions, and/or

(II) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or

(III) "Syntaxin-1" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Syntaxin-1" encoded by a nucleic acid that hybridizes to the "Syntaxin-1" nucleic acid or its complement under low stringency conditions, and/or

(III) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions, and/or

(IV) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or

(V) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(VI) "Zinc finger protein 198 " (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Zinc finger protein 198 " encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198 " nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:
(i) "ADAMTS-19" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

- (ii) "APLP1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Calsyntenin-1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (vii) "Calsyntenin-2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (viii) "Calsyntenin-3" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (ix) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes

to the "Chondroitin sulfate proteoglycan 6 " nucleic acid or its complement under low stringency conditions,

(x) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,

(xi) "DC6 protein" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,

(xii) "Dynein light chain 2A " (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xiii) "Dynein light chain-A " (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynein light chain-A " encoded by a nucleic acid that hybridizes to the "Dynein light chain-A " nucleic acid or its complement under low stringency conditions,

(xiv) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xv) "Eukaryotic translation initiation factor 4A, isoform " (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform " encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform " nucleic acid or its complement under low stringency conditions,

(xvi) "FLJ13910" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

- (xvii) "FRAP1" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,
- (xviii) "GTP-binding protein ERA" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,
- (xix) "HDAC2" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,
- (xx) "HERC2 protein" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xxi) "HSPC154" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xxii) "HSPC245" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xxiii) "IKAP" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0056" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA0166" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA0325" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0325" encoded by a nucleic acid that hybridizes to the "KIAA0325" nucleic acid or its complement under low stringency conditions,

(xxviii) "KIAA0564" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xxix) "KIAA0763" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxx) "LIB (leucine-rich repeat protein)" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Laminin, gamma 1 " (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xxxii) "MBIP" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xxxiii) "MEGF7" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEGF7" encoded by a nucleic acid that hybridizes to the "MEGF7" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Munc18-1" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Munc18-1" encoded by a nucleic acid that hybridizes to the "Munc18-1" nucleic acid or its complement under low stringency conditions,

(xxxv) "Myosin IXB" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xxxvi) "NIPSNAP1" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "NIPSNAP2" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Neurexin-1" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,

(xxxix) "PDZ and LIM domain protein 1" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xl) "PILT" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xli) "Paladin" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xlii) "Peroxiredoxin 4" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Peroxiredoxin 4" encoded by a nucleic acid that hybridizes to the "Peroxiredoxin 4" nucleic acid or its complement under low stringency conditions,

(xliii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(xliv) "Procollagen C-endopeptidase enhancer " (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Procollagen C-endopeptidase enhancer " encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer " nucleic acid or its complement under low stringency conditions,

(xlv) "Programmed cell death 10" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xlvi) "Protein similar to AGCP6688 " (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to AGCP6688 " encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688 " nucleic acid or its complement under low stringency conditions,

(xlvii) "RPGR-interacting protein 1" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,

(xlviii) "Reelin" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Reelin" encoded by a

nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(xlix) "Serine/threonine protein phosphatase 6 " (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6 " encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6 " nucleic acid or its complement under low stringency conditions,

(l) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(li) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lii) "Syntaxin-1" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Syntaxin-1" encoded by a nucleic acid that hybridizes to the "Syntaxin-1" nucleic acid or its complement under low stringency conditions,

(liii) "Ubiquitin-protein ligase E3-alpha " (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase E3-alpha " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha " nucleic acid or its complement under low stringency conditions,

(liv) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or (lvi) "Zinc finger protein 198 " (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homologue thereof, or a variant of "Zinc finger protein 198 " encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198 " nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

The invention further relates to the Presenilin 2 complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "DOCK3" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
 - (ii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and
 - (iii) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
 - (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
 - (ii) "200 kDa proteasome activator " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "200 kDa proteasome activator " encoded by a nucleic acid that hybridizes to the "200

kDa proteasome activator " nucleic acid or its complement under low stringency conditions,

(iii) "ADP-ribosylation factor 3" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 3" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 3" nucleic acid or its complement under low stringency conditions,

(iv) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,

(v) "ATP-dependent metalloprotease FtsH1 homologue " (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homologue " encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homologue " nucleic acid or its complement under low stringency conditions,

(vi) "Acetolactate synthase " (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetolactate synthase " encoded by a nucleic acid that hybridizes to the "Acetolactate synthase " nucleic acid or its complement under low stringency conditions,

(vii) "Adrenoleukodystrophy protein" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,

(viii) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(ix) "Calcium-binding protein P22" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

- (x) "Cation-chloride cotransporter-interacting protein " (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cation-chloride cotransporter-interacting protein " encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein " nucleic acid or its complement under low stringency conditions,
- (xi) "Centromere/kinetochore protein ZW10 homologue " (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Centromere/kinetochore protein ZW10 homologue " encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homologue " nucleic acid or its complement under low stringency conditions,
- (xii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xiii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions,
- (xiv) "Down syndrome critical region protein 2" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xv) "ECSIT" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420"

encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xviii) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xix) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xx) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxi) "HTRA2" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxii) "HU-K4 " (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103"

encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions,

(xxvii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xxviii) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxix) "NPD002 " (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NPD002 " encoded by a nucleic acid that hybridizes to the "NPD002 " nucleic acid or its complement under low stringency conditions,

(xxx) "P63 protein" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(xxxi) "PSMA1 " (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA1 " encoded by a nucleic acid that hybridizes to the "PSMA1 " nucleic acid or its complement under low stringency conditions,

(xxxii) "PSMA3 " (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA3 " encoded by a nucleic acid that hybridizes to the "PSMA3 " nucleic acid or its complement under low stringency conditions,

(xxxiii) "PSMA4" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(xxxiv) "PSMA6" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(xxxv) "PSMB1" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(xxxvi) "PSMB2" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(xxxvii) "PSMB3" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

(xxxviii) "PSMB4 " (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB4 " encoded by a nucleic acid that hybridizes to the "PSMB4 " nucleic acid or its complement under low stringency conditions,

(xxxix) "PSMB5" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(xl) "PSMB6" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(xli) "PSMC1" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(xlii) "PSMC2" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC2"

encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(xliii) "PSMC3" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(xliv) "PSMC4" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(xlv) "PSMC5" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(xlvi) "PSMC6" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(xlvii) "PSMD1" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(xlviii) "PSMD11" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(xlix) "PSMD12" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(l) "PSMD13" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

- (li) "PSMD2" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,
- (lii) "PSMD3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,
- (liii) "PSMD4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,
- (liv) "Prohibitin" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,
- (lv) "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " encoded by a nucleic acid that hybridizes to the "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " nucleic acid or its complement under low stringency conditions,
- (lvi) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,
- (lvii) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,
- (lviii) "Stearoyl-CoA desaturase " (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Stearoyl-CoA desaturase " encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase " nucleic acid or its complement under low stringency conditions, (lix) "Ubiquitin-protein ligase EDD " (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase EDD " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD " nucleic acid or its complement under low stringency conditions,

(lx) "Voltage-dependent anion channel 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and

(lxi) "Wolframin" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

2. The protein complex according to No. 1 wherein the first protein is the protein "Presenilin 2" (SEQ ID No:152), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that

hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "200 kDa proteasome activator " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "200 kDa proteasome activator " encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator " nucleic acid or its complement under low stringency conditions,

(iii) "ADP-ribosylation factor 3" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 3" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 3" nucleic acid or its complement under low stringency conditions,

(iv) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,

(v) "ATP-dependent metalloprotease FtsH1 homologue " (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homologue " encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homologue " nucleic acid or its complement under low stringency conditions,

(vi) "Acetolactate synthase " (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetolactate synthase " encoded by a nucleic acid that hybridizes to the "Acetolactate synthase " nucleic acid or its complement under low stringency conditions,

(vii) "Adrenoleukodystrophy protein" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,

(viii) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

- (ix) "Calcium-binding protein P22" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,
- (x) "Cation-chloride cotransporter-interacting protein " (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cation-chloride cotransporter-interacting protein " encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein " nucleic acid or its complement under low stringency conditions,
- (xi) "Centromere/kinetochore protein ZW10 homologue " (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Centromere/kinetochore protein ZW10 homologue " encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homologue " nucleic acid or its complement under low stringency conditions,
- (xii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xiii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions,
- (xiv) "DOCK3" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (xv) "Down syndrome critical region protein 2" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xvi) "ECSIT" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECSIT" encoded by a

nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xvii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xviii) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xix) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xx) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxii) "HTRA2" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxiii) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062"

encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions,

(xxviii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xxix) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxx) "NPD002 " (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NPD002 " encoded by a nucleic acid that hybridizes to the "NPD002 " nucleic acid or its complement under low stringency conditions,

(xxxi) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxxii) "P63 protein" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(xxxiii) "PSMA1 " (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA1 " encoded by a nucleic acid that hybridizes to the "PSMA1 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "PSMA3 " (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA3 " encoded by a nucleic acid that hybridizes to the "PSMA3 " nucleic acid or its complement under low stringency conditions,

(xxxv) "PSMA4" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(xxxvi) "PSMA6" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(xxxvii) "PSMB1" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(xxxviii) "PSMB2" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(xxxix) "PSMB3" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

(xl) "PSMB4 " (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB4 " encoded by a nucleic acid that hybridizes to the "PSMB4 " nucleic acid or its complement under low stringency conditions,

(xli) "PSMB5" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB5"

encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(xlii) "PSMB6" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(xliii) "PSMC1" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(xliv) "PSMC2" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(xlv) "PSMC3" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(xlvi) "PSMC4" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(xlvii) "PSMC5" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(xlviii) "PSMC6" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(xlix) "PSMD1" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

- (I) "PSMD11" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,
- (li) "PSMD12" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,
- (lii) "PSMD13" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,
- (liii) "PSMD2" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,
- (liv) "PSMD3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,
- (lv) "PSMD4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,
- (lvi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lvii) "Prohibitin" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,
- (lviii) "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment

thereof, or a homologue thereof, or a variant of "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " encoded by a nucleic acid that hybridizes to the "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " nucleic acid or its complement under low stringency conditions,

(lix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lx) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxi) "Stearoyl-CoA desaturase " (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stearoyl-CoA desaturase " encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase " nucleic acid or its complement under low stringency conditions,

(lixii) "Ubiquitin-protein ligase EDD " (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase EDD " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD " nucleic acid or its complement under low stringency conditions,

(lixiii) "Voltage-dependent anion channel 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(lixiv) "Wolframin" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 60 of the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "200 kDa proteasome activator " encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator " nucleic acid or its complement under low stringency conditions,
- (iii) "ADP-ribosylation factor 3" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 3" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 3" nucleic acid or its complement under low stringency conditions,
- (iv) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-dependent metalloprotease FtsH1 homologue " (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homologue " encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homologue " nucleic acid or its complement under low stringency conditions,
- (vi) "Acetolactate synthase " (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetolactate synthase " encoded by a nucleic acid that hybridizes to the "Acetolactate synthase " nucleic acid or its complement under low stringency conditions,
- (vii) "Adrenoleukodystrophy protein" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,

- (viii) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (ix) "Calcium-binding protein P22" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,
- (x) "Cation-chloride cotransporter-interacting protein " (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cation-chloride cotransporter-interacting protein " encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein " nucleic acid or its complement under low stringency conditions,
- (xi) "Centromere/kinetochore protein ZW10 homologue " (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Centromere/kinetochore protein ZW10 homologue " encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homologue " nucleic acid or its complement under low stringency conditions,
- (xii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xiii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions,
- (xiv) "DOCK3" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (xv) "Down syndrome critical region protein 2" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that

hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xvi) "ECSIT" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xvii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xviii) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xix) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xx) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxii) "HTRA2" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxiii) "HU-K4 " (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4 "

encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions,

(xxviii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xxix) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxx) "NPD002 " (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NPD002 " encoded by a nucleic acid that hybridizes to the "NPD002 " nucleic acid or its complement under low stringency conditions,

(xxxi) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (xxxii) "P63 protein" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "PSMA1 " (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA1 " encoded by a nucleic acid that hybridizes to the "PSMA1 " nucleic acid or its complement under low stringency conditions,
- (xxxiv) "PSMA3 " (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA3 " encoded by a nucleic acid that hybridizes to the "PSMA3 " nucleic acid or its complement under low stringency conditions,
- (xxxv) "PSMA4" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,
- (xxxvi) "PSMA6" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "PSMB1" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "PSMB2" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,
- (xxxix) "PSMB3" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,
- (xi) "PSMB4 " (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB4 "

encoded by a nucleic acid that hybridizes to the "PSMB4 " nucleic acid or its complement under low stringency conditions,

(xli) "PSMB5" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(xlii) "PSMB6" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(xliii) "PSMC1" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(xliv) "PSMC2" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(xlv) "PSMC3" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(xlvi) "PSMC4" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(xlvii) "PSMC5" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(xlviii) "PSMC6" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

- (xlix) "PSMD1" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,
- (l) "PSMD11" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,
- (li) "PSMD12" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,
- (lii) "PSMD13" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,
- (liii) "PSMD2" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,
- (liv) "PSMD3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,
- (lv) "PSMD4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,
- (lvi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lvii) "Prohibitin" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Prohibitin"

encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lviii) "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " encoded by a nucleic acid that hybridizes to the "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " nucleic acid or its complement under low stringency conditions,

(lix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lx) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxi) "Stearoyl-CoA desaturase " (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stearoyl-CoA desaturase " encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase " nucleic acid or its complement under low stringency conditions,

(lxii) "Ubiquitin-protein ligase EDD " (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase EDD " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD " nucleic acid or its complement under low stringency conditions,

(lxiii) "Voltage-dependent anion channel 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxiv) "Wolframin" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Wolframin"

encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Presenilin 2 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Presenilin 2 complex selected from

- (i) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (ii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (iii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions,
- (iv) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555"

encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(vii) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(x) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xi) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions,

(xii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and

(xiii) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5

hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (ii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (iii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions,
- (iv) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420"

encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(vi) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(vii) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(x) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xi) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions,

(xii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or

(xiii) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (ii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (iii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions,
- (iv) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678"

encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(x) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xi) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions,

(xii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or

(xiii) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, comprising the steps of:

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

(a) exposing said complex, or a cell or organism containing Presenilin 2 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

- (ii) "200 kDa proteasome activator " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "200 kDa proteasome activator " encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator " nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ADP-ribosylation factor 3" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 3" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "ATP-dependent metalloprotease FtsH1 homologue " (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homologue " encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homologue " nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Acetolactate synthase " (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetolactate synthase " encoded by a nucleic acid that hybridizes to the "Acetolactate synthase " nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Adrenoleukodystrophy protein" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or

- (ix) "Calcium-binding protein P22" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Cation-chloride cotransporter-interacting protein " (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cation-chloride cotransporter-interacting protein " encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein " nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Centromere/kinetochore protein ZW10 homologue " (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Centromere/kinetochore protein ZW10 homologue " encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homologue " nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "DOCK3" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Down syndrome critical region protein 2" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "ECSIT" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECSIT" encoded by a

nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or

(xix) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or

(xx) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "HTRA2" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "HU-K4 " (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062"

encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or

(xxix) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "NPD002 " (SEQ ID No:127) or a functionally active derivative thereof; or a functionally active fragment thereof, or a homologue thereof, or a variant of "NPD002 " encoded by a nucleic acid that hybridizes to the "NPD002 " nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "P63 protein" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "PSMA1 " (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA1 " encoded by a nucleic acid that hybridizes to the "PSMA1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "PSMA3 " (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA3 " encoded by a nucleic acid that hybridizes to the "PSMA3 " nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "PSMA4" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "PSMA6" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "PSMB1" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "PSMB2" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "PSMB3" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or

(xl) "PSMB4 " (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB4 " encoded by a nucleic acid that hybridizes to the "PSMB4 " nucleic acid or its complement under low stringency conditions, and/or

(xli) "PSMB5" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB5"

encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "PSMB6" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "PSMC1" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "PSMC2" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "PSMC3" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "PSMC4" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "PSMC5" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "PSMC6" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "PSMD1" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or

- (i) "PSMD11" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "PSMD12" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "PSMD13" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PSMD2" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PSMD3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions, and/or
- (lv) "PSMD4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "Prohibitin" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment

thereof, or a homologue thereof, or a variant of "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " encoded by a nucleic acid that hybridizes to the "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " nucleic acid or its complement under low stringency conditions, and/or

(lix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lx) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxi) "Stearoyl-CoA desaturase " (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stearoyl-CoA desaturase " encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase " nucleic acid or its complement under low stringency conditions, and/or

(lxii) "Ubiquitin-protein ligase EDD " (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase EDD " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD " nucleic acid or its complement under low stringency conditions, and/or

(lxiii) "Voltage-dependent anion channel 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(lxiv) "Wolframin" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said

complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

(ii) "200 kDa proteasome activator " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "200 kDa proteasome activator " encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator " nucleic acid or its complement under low stringency conditions, and/or

(iii) "ADP-ribosylation factor 3" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 3" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 3" nucleic acid or its complement under low stringency conditions, and/or

(iv) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or

(v) "ATP-dependent metalloprotease FtsH1 homologue " (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homologue " encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homologue " nucleic acid or its complement under low stringency conditions, and/or

- (vi) "Acetolactate synthase " (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetolactate synthase " encoded by a nucleic acid that hybridizes to the "Acetolactate synthase " nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Adrenoleukodystrophy protein" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Calcium-binding protein P22" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Cation-chloride cotransporter-interacting protein " (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cation-chloride cotransporter-interacting protein " encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein " nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Centromere/kinetochore protein ZW10 homologue " (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Centromere/kinetochore protein ZW10 homologue " encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homologue " nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions, and/or

(xiv) "DOCK3" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Down syndrome critical region protein 2" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "ECSIT" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or

(xix) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or

(xx) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-

beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "HTRA2" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "HU-K4 " (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or

(xxix) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3"

encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "NPD002 " (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NPD002 " encoded by a nucleic acid that hybridizes to the "NPD002 " nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "P63 protein" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "PSMA1 " (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA1 " encoded by a nucleic acid that hybridizes to the "PSMA1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "PSMA3 " (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA3 " encoded by a nucleic acid that hybridizes to the "PSMA3 " nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "PSMA4" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "PSMA6" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "PSMB1" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or

- (xxxviii) "PSMB2" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or
- (xxxix) "PSMB3" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or
- (xl) "PSMB4 " (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB4 " encoded by a nucleic acid that hybridizes to the "PSMB4 " nucleic acid or its complement under low stringency conditions, and/or
- (xli) "PSMB5" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "PSMB6" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or
- (xlili) "PSMC1" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or
- (xliv) "PSMC2" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or
- (xlv) "PSMC3" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or
- (xlvi) "PSMC4" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC4"

encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "PSMC5" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "PSMC6" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "PSMD1" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or

(l) "PSMD11" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or

(ii) "PSMD12" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or

(iii) "PSMD13" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or

(liii) "PSMD2" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or

(liv) "PSMD3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions, and/or

(Iv) "PSMD4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or

(Ivi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(Ivii) "Prohibitin" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or

(Iviii) "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " encoded by a nucleic acid that hybridizes to the "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " nucleic acid or its complement under low stringency conditions, and/or

(lix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(Ix) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(Ixi) "Stearoyl-CoA desaturase " (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stearoyl-CoA desaturase " encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase " nucleic acid or its complement under low stringency conditions, and/or

(Ixii) "Ubiquitin-protein ligase EDD " (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase EDD " encoded by a nucleic acid that hybridizes to the

"Ubiquitin-protein ligase EDD " nucleic acid or its complement under low stringency conditions, and/or

(Ixiii) "Voltage-dependent anion channel 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(Ixiv) "Wolframin" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "200 kDa proteasome activator " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "200 kDa proteasome activator " encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator " nucleic acid or its complement under low stringency conditions,

(iii) "ADP-ribosylation factor 3" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 3" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 3" nucleic acid or its complement under low stringency conditions,

(iv) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,

(v) "ATP-dependent metalloprotease FtsH1 homologue " (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homologue " encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homologue " nucleic acid or its complement under low stringency conditions,

(vi) "Acetolactate synthase " (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Acetolactate synthase " encoded by a nucleic acid that hybridizes to the "Acetolactate synthase " nucleic acid or its complement under low stringency conditions,

(vii) "Adrenoleukodystrophy protein" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,

(viii) "CGI-51" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(ix) "Calcium-binding protein P22" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(x) "Cation-chloride cotransporter-interacting protein " (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cation-chloride cotransporter-interacting protein " encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein " nucleic acid or its complement under low stringency conditions,

(xi) "Centromere/kinetochore protein ZW10 homologue " (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Centromere/kinetochore protein ZW10 homologue " encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homologue " nucleic acid or its complement under low stringency conditions,

(xii) "Cerebral protein 10" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xiii) "DKFZp586c1924 " (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DKFZp586c1924 " encoded by a nucleic acid that hybridizes to the "DKFZp586c1924 " nucleic acid or its complement under low stringency conditions,

- (xiv) "DOCK3" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (xv) "Down syndrome critical region protein 2" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xvi) "ECSIT" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ20420" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (xix) "FLJ22555" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (xx) "FLJ22678" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (xxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the

"Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxii) "HTRA2" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxiii) "HU-K4 " (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(xxv) "KIAA0090" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xxvi) "KIAA0103" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA1499" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1499" encoded by a nucleic acid that hybridizes to the "KIAA1499" nucleic acid or its complement under low stringency conditions,

(xxviii) "MGC4248 " (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xxix) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxx) "NPD002 " (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NPD002 " encoded by a nucleic acid that hybridizes to the "NPD002 " nucleic acid or its complement under low stringency conditions,

(xxxi) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxxii) "P63 protein" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(xxxiii) "PSMA1 " (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA1 " encoded by a nucleic acid that hybridizes to the "PSMA1 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "PSMA3 " (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA3 " encoded by a nucleic acid that hybridizes to the "PSMA3 " nucleic acid or its complement under low stringency conditions,

(xxxv) "PSMA4" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(xxxvi) "PSMA6" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(xxxvii) "PSMB1" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(xxxviii) "PSMB2" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB2"

encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(xxxix) "PSMB3" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

(xli) "PSMB4 " (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB4 " encoded by a nucleic acid that hybridizes to the "PSMB4 " nucleic acid or its complement under low stringency conditions,

(xlii) "PSMB5" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(xliii) "PSMB6" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(xliv) "PSMC1" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(xlv) "PSMC2" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(xlvi) "PSMC3" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(xlvii) "PSMC4" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(xlvii) "PSMC5" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(xlviii) "PSMC6" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(xlix) "PSMD1" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(i) "PSMD11" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(ii) "PSMD12" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(iii) "PSMD13" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(liii) "PSMD2" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(liv) "PSMD3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lv) "PSMD4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PSMD4" encoded by a

nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lvi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lvii) "Prohibitin" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lviii) "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " encoded by a nucleic acid that hybridizes to the "Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3 " nucleic acid or its complement under low stringency conditions,

(lix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lx) "Sortilin 1" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxi) "Stearoyl-CoA desaturase " (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stearoyl-CoA desaturase " encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase " nucleic acid or its complement under low stringency conditions,

(lxii) "Ubiquitin-protein ligase EDD " (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Ubiquitin-protein ligase EDD " encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD " nucleic acid or its complement under low stringency conditions,

(Ixiii) "Voltage-dependent anion channel 2" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or (Ixiv) "Wolframin" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the Nicastrin complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
 - (ii) "BACE1" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
 - (iii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
 - (iv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (v) "Presenilin-1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and
- (vi) "Presenilin-2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (iv) "BSCv protein" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BSCv protein" encoded by a nucleic acid that hybridizes to the "BSCv protein" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (vi) "Casein kinase II beta chain " (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Casein kinase II beta chain " encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain " nucleic acid or its complement under low stringency conditions,
- (vii) "Cathepsin B" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
- (viii) "Delta-6 fatty acid desaturase " (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,
- (ix) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13977" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xi) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xii) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xiii) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xiv) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions,

(xv) "ICAM-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xvi) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions,

(xviii) "Mesenchymal stem cell protein DSCD75 " (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75 " encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75 " nucleic acid or its complement under low stringency conditions,

(xix) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xx) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxi) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions,

(xxii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxiii) "Protein similar to stromal cell-derived factor 2 " (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to stromal cell-derived factor 2 " encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2 " nucleic acid or its complement under low stringency conditions,

(xxiv) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,

(xxv) "REP8 protein " (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REP8 protein " encoded by a nucleic acid that hybridizes to the "REP8 protein " nucleic acid or its complement under low stringency conditions,

(xxvi) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions,

(xxvii) "Retinal short-chain dehydrogenase/reductase retSDR2 " (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2 " encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2 " nucleic acid or its complement under low stringency conditions,

(xxviii) "Stromal cell-derived factor 2-like 1 " (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1 " encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1 " nucleic acid or its complement under low stringency conditions,

(xxix) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and

(xxx) "Voltage-dependent anion channel 1" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 1" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 1" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. The protein complex according to No. 1 wherein the first protein is the protein "Nicastrin" (SEQ ID No:14), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a

nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "BACE1" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,

(vi) "BSCv protein" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BSCv protein" encoded by a nucleic acid that hybridizes to the "BSCv protein" nucleic acid or its complement under low stringency conditions,

(vii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(viii) "Casein kinase II beta chain " (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Casein kinase II beta chain " encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain " nucleic acid or its complement under low stringency conditions,

(ix) "Cathepsin B" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(x) "Delta-6 fatty acid desaturase " (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,

(xi) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(xii) "FLJ13977" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,

(xiii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xiv) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

(xv) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(xvi) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions,

(xvii) "ICAM-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181"

encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions,

(xix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions,

(xx) "Mesenchymal stem cell protein DSCD75 " (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75 " encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75 " nucleic acid or its complement under low stringency conditions,

(xxi) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxiv) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions,

(xxv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxvi) "Presenilin-1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-1"

encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxvii) "Presenilin-2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to stromal cell-derived factor 2 " (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to stromal cell-derived factor 2 " encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2 " nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,

(xxxi) "REP8 protein " (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REP8 protein " encoded by a nucleic acid that hybridizes to the "REP8 protein " nucleic acid or its complement under low stringency conditions,

(xxxii) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions,

(xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2 " (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2 " encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "Stromal cell-derived factor 2-like 1 " (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1 " encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1 " nucleic acid or its complement under low stringency conditions,

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Voltage-dependent anion channel 1" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 1" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 1" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 29 of the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

- (iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v) "BACE1" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (vi) "BSCv protein" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BSCv protein" encoded by a nucleic acid that hybridizes to the "BSCv protein" nucleic acid or its complement under low stringency conditions,
- (vii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (viii) "Casein kinase II beta chain " (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Casein kinase II beta chain " encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain " nucleic acid or its complement under low stringency conditions,
- (ix) "Cathepsin B" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
- (x) "Delta-6 fatty acid desaturase " (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,
- (xi) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (xii) "FLJ13977" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13977"

encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,

(xiii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xiv) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

(xv) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(xvi) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions,

(xvii) "ICAM-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions,

(xix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions,

(xx) "Mesenchymal stem cell protein DSCD75 " (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "Mesenchymal stem cell protein DSCD75 " encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75 " nucleic acid or its complement under low stringency conditions,

(xxi) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxiv) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions,

(xxv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxvi) "Presenilin-1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxvii) "Presenilin-2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic

acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to stromal cell-derived factor 2 " (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to stromal cell-derived factor 2 " encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2 " nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,

(xxxi) "REP8 protein " (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REP8 protein " encoded by a nucleic acid that hybridizes to the "REP8 protein " nucleic acid or its complement under low stringency conditions,

(xxxii) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions,

(xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2 " (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2 " encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "Stromal cell-derived factor 2-like 1 " (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1 " encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1 " nucleic acid or its complement under low stringency conditions,

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that

hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Voltage-dependent anion channel 1" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 1" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 1" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:
expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell,
isolating the protein complex which is attached to the bait protein, and optionally
dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Nicastrin complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the Nicastrin complex selected from
- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
 - (ii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
 - (iii) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
 - (iv) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

- (v) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions,
- (x) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions,
- (xi) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions, and
- (xii) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement

under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

- (iv) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions,
- (x) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions,
- (xi) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions, and/or

(xii) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (iv) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

- (vi) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions,
- (x) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions,
- (xi) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, comprising the steps of:
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing Nicastrin complex to one or more candidate molecules; and
 - (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(v) "BACE1" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "BSCv protein" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BSCv protein" encoded by a nucleic acid that hybridizes to the "BSCv protein" nucleic acid or its complement under low stringency conditions, and/or

(vii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Casein kinase II beta chain " (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Casein kinase II beta chain " encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain " nucleic acid or its complement under low stringency conditions, and/or

- (ix) "Cathepsin B" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Delta-6 fatty acid desaturase " (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "FLJ13977" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical

protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions, and/or

(xvii) "ICAM-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions, and/or

(xix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Mesenchymal stem cell protein DSCD75 " (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75 " encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75 " nucleic acid or its complement under low stringency conditions, and/or

(xxi) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1,

regulatory subunit 15B " nucleic acid or its complement under low stringency conditions, and/or

(xxv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "Presenilin-1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Presenilin-2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "Protein similar to stromal cell-derived factor 2 " (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to stromal cell-derived factor 2 " encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2 " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "REP8 protein " (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REP8 protein " encoded by a nucleic acid that hybridizes to the "REP8 protein " nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions, and/or (xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2 " (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2 " encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Stromal cell-derived factor 2-like 1 " (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1 " encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Voltage-dependent anion channel 1" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 1" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BACE1" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "BSCv protein" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BSCv protein" encoded by a nucleic acid that hybridizes to the "BSCv protein" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Casein kinase II beta chain " (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Casein kinase II beta chain " encoded by a nucleic acid that hybridizes to the "Casein

kinase II beta chain " nucleic acid or its complement under low stringency conditions, and/or

(ix) "Cathepsin B" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or

(x) "Delta-6 fatty acid desaturase " (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions, and/or

(xi) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or

(xii) "FLJ13977" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or

(xv) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions, and/or

(xvii) "ICAM-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions, and/or

(xix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Mesenchymal stem cell protein DSCD75 " (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75 " encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75 " nucleic acid or its complement under low stringency conditions, and/or

(xxi) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions, and/or

(xxv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "Presenilin-1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Presenilin-2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "Protein similar to stromal cell-derived factor 2 " (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to stromal cell-derived factor 2 " encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2 " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "REP8 protein " (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REP8

protein " encoded by a nucleic acid that hybridizes to the "REP8 protein " nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2 " (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2 " encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Stromal cell-derived factor 2-like 1 " (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1 " encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Voltage-dependent anion channel 1" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 1" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v) "BACE1" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (vi) "BSCv protein" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BSCv protein" encoded by a nucleic acid that hybridizes to the "BSCv protein" nucleic acid or its complement under low stringency conditions,
- (vii) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (viii) "Casein kinase II beta chain " (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Casein kinase II beta chain " encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain " nucleic acid or its complement under low stringency conditions,
- (ix) "Cathepsin B" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
- (x) "Delta-6 fatty acid desaturase " (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-6 fatty acid desaturase " encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase " nucleic acid or its complement under low stringency conditions,

- (xi) "ENSG00000144840" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (xii) "FLJ13977" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xiii) "FLJ20342" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xiv) "FLJ20481" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xv) "FLJ22390" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein tyrosine phosphatase ensg00000149185 " (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Hypothetical protein tyrosine phosphatase ensg00000149185 " encoded by a nucleic acid that hybridizes to the "Hypothetical protein tyrosine phosphatase ensg00000149185 " nucleic acid or its complement under low stringency conditions,
- (xvii) "ICAM-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA1181" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1181" encoded by a nucleic acid that hybridizes to the "KIAA1181" nucleic acid or its complement under low stringency conditions,

- (xix) "KIAA1533" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1533" encoded by a nucleic acid that hybridizes to the "KIAA1533" nucleic acid or its complement under low stringency conditions,
- (xx) "Mesenchymal stem cell protein DSCD75 " (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75 " encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75 " nucleic acid or its complement under low stringency conditions,
- (xxi) "NICE-3" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xxii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xxiv) "PP1, regulatory subunit 15B " (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP1, regulatory subunit 15B " encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B " nucleic acid or its complement under low stringency conditions,
- (xxv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xxvi) "Presenilin-1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxvii) "Presenilin-2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to stromal cell-derived factor 2 " (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein similar to stromal cell-derived factor 2 " encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2 " nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,

(xxxi) "REP8 protein " (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REP8 protein " encoded by a nucleic acid that hybridizes to the "REP8 protein " nucleic acid or its complement under low stringency conditions,

(xxxii) "RING finger protein 5 " (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RING finger protein 5 " encoded by a nucleic acid that hybridizes to the "RING finger protein 5 " nucleic acid or its complement under low stringency conditions,

(xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2 " (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2 " encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "Stromal cell-derived factor 2-like 1 " (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "Stromal cell-derived factor 2-like 1 " encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1 " nucleic acid or its complement under low stringency conditions,

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or(xxxvi) "Voltage-dependent anion channel 1" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 1" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 1" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the Aph-1a complex:

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(iii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (iv) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
 - (v) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and
 - (vi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
 - (ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
 - (iii) "Brain-specific GTP-binding protein " (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Brain-specific GTP-binding protein " encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein " nucleic acid or its complement under low stringency conditions,
 - (iv) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (v) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions,
- (vi) "Dihydrofolate reductase " (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dihydrofolate reductase " encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase " nucleic acid or its complement under low stringency conditions,
- (vii) "Endocytic receptor Endo180" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ13660" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (ix) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (x) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,
- (xi) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,
- (xii) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions,

- (xiii) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xvi) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xvii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xviii) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (xix) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions,
- (xx) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions,

(xxi) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,

(xxii) "RAB-18" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,

(xxiii) "Rab3 GTPase-activating protein, non-catalytic subunit " (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit " encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit " nucleic acid or its complement under low stringency conditions,

(xxiv) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxv) "SMAP-1B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(xxvi) "Sideroflexin 1" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(xxvii) "Signal transducer and activator of transcription-1 " (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Signal transducer and activator of transcription-1 " encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1 " nucleic acid or its complement under low stringency conditions,

(xxviii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xxix) "Sterol O-acyltransferase 1 " (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterol O-acyltransferase 1 " encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1 " nucleic acid or its complement under low stringency conditions,

(xxx) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions,

(xxxi) "Triple functional domain protein (PTPRF interacting) " (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Triple functional domain protein (PTPRF interacting) " encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting) " nucleic acid or its complement under low stringency conditions, and

(xxxii) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

2. The protein complex according to No. 1 wherein the first protein is the protein "Aph-1a" (SEQ ID No:2), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "Brain-specific GTP-binding protein " (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Brain-specific GTP-binding protein " encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein " nucleic acid or its complement under low stringency conditions,

(vi) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (vii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions,
- (viii) "Dihydrofolate reductase " (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dihydrofolate reductase " encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase " nucleic acid or its complement under low stringency conditions,
- (ix) "Endocytic receptor Endo180" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13660" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xi) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xii) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,
- (xiii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions,

- (xv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xviii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xix) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xx) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xxi) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (xxii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (xxiii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xxv) "Protocadherin 7" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (xxvi) "Protocadherin beta 16" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (xxvii) "Protocadherin beta 8" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (xxviii) "RAB-18" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (xxix) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,
- (xxx) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain

dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxi) "SMAP-1B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(xxxii) "Sideroflexin 1" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Signal transducer and activator of transcription-1 " (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Signal transducer and activator of transcription-1 " encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xxxv) "Sterol O-acyltransferase 1 " (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterol O-acyltransferase 1 " encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions,

(xxxvii) "Triple functional domain protein (PTPRF interacting) " (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Triple functional domain protein (PTPRF interacting) " encoded by a nucleic acid that hybridizes to the "Triple functional domain protein

(PTPRF interacting) " nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 31 of the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "Brain-specific GTP-binding protein " (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Brain-specific GTP-binding protein " encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein " nucleic acid or its complement under low stringency conditions,

- (vi) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (vii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions,
- (viii) "Dihydrofolate reductase " (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dihydrofolate reductase " encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase " nucleic acid or its complement under low stringency conditions,
- (ix) "Endocytic receptor Endo180" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13660" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xi) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xii) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,
- (xiii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

- (xiv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xviii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xix) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xx) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xxi) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,

- (xxii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xxv) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions,
- (xxvi) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions,
- (xxvii) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,
- (xxviii) "RAB-18" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (xxix) "Rab3 GTPase-activating protein, non-catalytic subunit " (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit " encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit " nucleic acid or its complement under low stringency conditions,

(xxx) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxi) "SMAP-1B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(xxxii) "Sideroflexin 1" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Signal transducer and activator of transcription-1 " (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Signal transducer and activator of transcription-1 " encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xxxv) "Sterol O-acyltransferase 1 " (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterol O-acyltransferase 1 " encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions,

(xxxvii) "Triple functional domain protein (PTPRF interacting) " (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Triple functional domain protein (PTPRF interacting) " encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting) " nucleic acid or its complement under low stringency conditions, (xxxviii) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding

the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Aph-1a complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Aph-1a complex selected from

(i) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(ii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions,

(iii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,

(iv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251"

encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions,

(v) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,

(vi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(vii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(viii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(ix) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions,

(x) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions,

(xi) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,

(xii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase

retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xiv) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions, and

(xv) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

(a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being

selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (ii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions,
- (iii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions,
- (v) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

- (viii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (ix) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions,
- (x) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions,
- (xi) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,
- (xii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (xiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,
- (xiv) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions, and/or

(xv) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (ii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions,
- (iii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions,
- (v) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,

variant of "Brain-specific GTP-binding protein " encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein " nucleic acid or its complement under low stringency conditions, and/or

(vi) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions, and/or

(viii) "Dihydrofolate reductase " (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dihydrofolate reductase " encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase " nucleic acid or its complement under low stringency conditions, and/or

(ix) "Endocytic receptor Endo180" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(x) "FLJ13660" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xi) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions, and/or

27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.
29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
31. The method of No. 30, wherein said determining step comprises determining whether
- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
 - (iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
 - (iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
 - (v) "Brain-specific GTP-binding protein " (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein"

nucleic acid or its complement under low stringency conditions,

(xiv) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions, and/or

(xv) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions, comprising the steps of:

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

- (a) exposing said complex, or a cell or organism containing Aph-1a complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

- (vi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (viii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (ix) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions,
- (x) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions,
- (xi) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,
- (xii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (xiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a

- (xiii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

- (xxi) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions, and/or
- (xxviii) "RAB-18" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or
- (xxix) "Rab3 GTPase-activating protein, non-catalytic subunit " (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homologue thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit " encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "SMAP-1B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Sideroflexin 1" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Signal transducer and activator of transcription-1 " (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Signal transducer and activator of transcription-1 " encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Sterol O-acyltransferase 1 " (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterol O-acyltransferase 1 " encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Triple functional domain protein (PTPRF interacting) " (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Triple functional domain protein (PTPRF interacting) " encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting) " nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or

disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether
(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
(ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a

nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

(iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(v) "Brain-specific GTP-binding protein " (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Brain-specific GTP-binding protein " encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein " nucleic acid or its complement under low stringency conditions, and/or

(vi) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions, and/or

(viii) "Dihydrofolate reductase " (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dihydrofolate reductase " encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase " nucleic acid or its complement under low stringency conditions, and/or

(ix) "Endocytic receptor Endo180" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(x) "FLJ13660" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13660"

encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xi) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions, and/or

(xiii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions, and/or

(xv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that

hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "RAB-18" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "Rab3 GTPase-activating protein, non-catalytic subunit " (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit " encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "SMAP-1B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Sideroflexin 1" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Signal transducer and activator of transcription-1 " (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Signal transducer and activator of transcription-1 " encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Sterol O-acyltransferase 1 " (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterol O-acyltransferase 1 " encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1 " nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Triple functional domain protein (PTPRF interacting) " (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Triple functional domain protein (PTPRF interacting) " encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting) " nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

- (xi) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xii) "Integral membrane protein 2B (ITM2B) " (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B) " encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B) " nucleic acid or its complement under low stringency conditions,
- (xiii) "KIAA0062" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0062" encoded by a nucleic acid that hybridizes to the "KIAA0062" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0251" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0251" encoded by a nucleic acid that hybridizes to the "KIAA0251" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0971" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA1250" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xviii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

- (iii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v) "Brain-specific GTP-binding protein " (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Brain-specific GTP-binding protein " encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein " nucleic acid or its complement under low stringency conditions,
- (vi) "CGI-13" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (vii) "Cerebral protein-10 " (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Cerebral protein-10 " encoded by a nucleic acid that hybridizes to the "Cerebral protein-10 " nucleic acid or its complement under low stringency conditions,
- (viii) "Dihydrofolate reductase " (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dihydrofolate reductase " encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase " nucleic acid or its complement under low stringency conditions,
- (ix) "Endocytic receptor Endo180" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13660" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

"Protocadherin beta 8 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8 " nucleic acid or its complement under low stringency conditions,

(xxviii) "RAB-18" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,

(xxix) "Rab3 GTPase-activating protein, non-catalytic subunit " (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit " encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit " nucleic acid or its complement under low stringency conditions,

(xxx) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxi) "SMAP-1B" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(xxxii) "Sideroflexin 1" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Signal transducer and activator of transcription-1 " (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Signal transducer and activator of transcription-1 " encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a

- (xix) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xx) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xxi) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (xxii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xxv) "Protocadherin 7 " (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin 7 " encoded by a nucleic acid that hybridizes to the "Protocadherin 7 " nucleic acid or its complement under low stringency conditions,
- (xxvi) "Protocadherin beta 16 " (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 16 " encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16 " nucleic acid or its complement under low stringency conditions,
- (xxvii) "Protocadherin beta 8 " (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xxxv) "Sterol O-acyltransferase 1 " (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Sterol O-acyltransferase 1 " encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "Thioredoxin domain-containing protein " (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Thioredoxin domain-containing protein " encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein " nucleic acid or its complement under low stringency conditions,

(xxxvii) "Triple functional domain protein (PTPRF interacting) " (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Triple functional domain protein (PTPRF interacting) " encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting) " nucleic acid or its complement under low stringency conditions,

and/or(xxxviii) "Vacuolar ATP synthase membrane sector associated protein m8-9 " (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9 " encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9 " nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the Aph-1b complex:

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "Aph-1b" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1b" encoded by a

encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions,

(xii) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xiii) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,

(xiv) "PAS domain containing serine/threonine kinase" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xv) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,

(xvi) "Polycystin 2" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Polycystin 2" encoded by a nucleic acid that hybridizes to the "Polycystin 2" nucleic acid or its complement under low stringency conditions,

(xvii) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions,

(xviii) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions,

(xix) "Voltage-dependent anion channel 3" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(iv) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(v) "Activating transcription factor 6" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Activating transcription factor 6" encoded by a nucleic acid that hybridizes to the "Activating transcription factor 6" nucleic acid or its complement under low stringency conditions,

(vi) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(vii) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions,

(viii) "Calsyntenin 1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,

(ix) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(x) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions,

(xi) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560"

nucleic acid that hybridizes to the "Aph-1b" nucleic acid or its complement under low stringency conditions,

(ii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(iii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(iv) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and

(v) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase subunit" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "23 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a

variant of "Voltage-dependent anion channel 3" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 3" nucleic acid or its complement under low stringency conditions, and

(xx) "cAMP responsive element binding protein-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "cAMP responsive element binding protein-like 1" encoded by a nucleic acid that hybridizes to the "cAMP responsive element binding protein-like 1" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. The protein complex according to No. 1 wherein the first protein is the protein "Aph-1b" (SEQ ID No:208), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1b" encoded by a nucleic acid that hybridizes to the "Aph-1b" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase subunit" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "23 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue

thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(iv) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(v) "Activating transcription factor 6" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Activating transcription factor 6" encoded by a nucleic acid that hybridizes to the "Activating transcription factor 6" nucleic acid or its complement under low stringency conditions,

(vi) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(vii) "Aph-1b" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1b" encoded by a nucleic acid that hybridizes to the "Aph-1b" nucleic acid or its complement under low stringency conditions,

(viii) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin 1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,

(x) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

- (xi) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions,
- (xii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions,
- (xiii) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (xv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,
- (xvii) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (xviii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (xix) "Polycystin 2" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Polycystin 2" encoded by a nucleic acid that hybridizes to the "Polycystin 2" nucleic acid or its complement under low stringency conditions,
- (xx) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xxi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xxii) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions,
- (xxiv) "Voltage-dependent anion channel 3" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 3" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 3" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "cAMP responsive element binding protein-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "cAMP responsive element binding protein-like 1" encoded by a nucleic acid that hybridizes to the "cAMP responsive element binding protein-like 1" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 19 of the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase subunit" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "23 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (iv) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (v) "Activating transcription factor 6" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Activating transcription factor 6" encoded by a nucleic acid that hybridizes to the "Activating transcription factor 6" nucleic acid or its complement under low stringency conditions,
- (vi) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (vii) "Aph-1b" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1b" encoded by a nucleic acid that hybridizes to the "Aph-1b" nucleic acid or its complement under low stringency conditions,
- (viii) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin 1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,

(x) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(xi) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions,

(xii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions,

(xiii) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xiv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,

(xv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a

nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xvii) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,

(xviii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xix) "Polycystin 2" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Polycystin 2" encoded by a nucleic acid that hybridizes to the "Polycystin 2" nucleic acid or its complement under low stringency conditions,

(xx) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xxi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(xxii) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions,

(xxiii) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions,

(xxiv) "Voltage-dependent anion channel 3" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 3" encoded by a nucleic acid that hybridizes

to the "Voltage-dependent anion channel 3" nucleic acid or its complement under low stringency conditions,

(xxv) "cAMP responsive element binding protein-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "cAMP responsive element binding protein-like 1" encoded by a nucleic acid that hybridizes to the "cAMP responsive element binding protein-like 1" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Aph-1b complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Aph-1b complex selected from

(i) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions,

(iii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions,

(iv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,

(v) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions, and

(vi) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or

functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions,

- (ii) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (v) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions,

- (ii) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions,
- (iv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (v) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions, comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

- (a) exposing said complex, or a cell or organism containing Aph-1b complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the

presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

(ii) "23 kDa microsomal signal peptidase subunit" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "23 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(iii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue

thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

(iv) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(v) "Activating transcription factor 6" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Activating transcription factor 6" encoded by a nucleic acid that hybridizes to the "Activating transcription factor 6" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Aph-1b" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1b" encoded by a nucleic acid that hybridizes to the "Aph-1b" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Calsyntenin 1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions, and/or

(x) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or

- (xi) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

- (xix) "Polycystin 2" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Polycystin 2" encoded by a nucleic acid that hybridizes to the "Polycystin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "Voltage-dependent anion channel 3" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 3" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 3" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "cAMP responsive element binding protein-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "cAMP responsive element binding protein-like 1" encoded by a nucleic acid that hybridizes to the "cAMP responsive element binding protein-like 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said

complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether:

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
- (ii) "23 kDa microsomal signal peptidase subunit" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "23 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
- (iv) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Activating transcription factor 6" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Activating transcription factor 6" encoded by a nucleic acid that hybridizes to the "Activating transcription factor 6" nucleic acid or its complement under low stringency conditions, and/or

- (vi) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Aph-1b" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1b" encoded by a nucleic acid that hybridizes to the "Aph-1b" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Calsyntenin 1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

- (xiv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Polycystin 2" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Polycystin 2" encoded by a nucleic acid that hybridizes to the "Polycystin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Voltage-dependent anion channel 3" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 3" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 3" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "cAMP responsive element binding protein-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "cAMP responsive element binding protein-like 1" encoded by a nucleic acid that hybridizes to the "cAMP responsive element binding protein-like 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi

(siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase subunit" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "23 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit " (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "25 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(iv) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

- (v) "Activating transcription factor 6" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Activating transcription factor 6" encoded by a nucleic acid that hybridizes to the "Activating transcription factor 6" nucleic acid or its complement under low stringency conditions,
- (vi) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (vii) "Aph-1b" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1b" encoded by a nucleic acid that hybridizes to the "Aph-1b" nucleic acid or its complement under low stringency conditions,
- (viii) "Autocrine motility factor receptor" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Autocrine motility factor receptor" encoded by a nucleic acid that hybridizes to the "Autocrine motility factor receptor" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin 1" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsyntenin 1" encoded by a nucleic acid that hybridizes to the "Calsyntenin 1" nucleic acid or its complement under low stringency conditions,
- (x) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (xi) "FLJ10737" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10737" encoded by a nucleic acid that hybridizes to the "FLJ10737" nucleic acid or its complement under low stringency conditions,
- (xii) "FLJ14560" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ14560" encoded by a nucleic acid that hybridizes to the "FLJ14560" nucleic acid or its complement under low stringency conditions,

- (xiii) "HU-K4" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0363" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0363" encoded by a nucleic acid that hybridizes to the "KIAA0363" nucleic acid or its complement under low stringency conditions,
- (xv) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,
- (xvii) "PP2C gamma" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (xviii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xix) "Polycystin 2" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Polycystin 2" encoded by a nucleic acid that hybridizes to the "Polycystin 2" nucleic acid or its complement under low stringency conditions,
- (xx) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xxi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(xxii) "Protocadherin beta 8a" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 8a" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8a" nucleic acid or its complement under low stringency conditions,

(xxiii) "Protocadherin gamma C3 " (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3 " encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3 " nucleic acid or its complement under low stringency conditions,

(xxiv) "Voltage-dependent anion channel 3" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Voltage-dependent anion channel 3" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 3" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "cAMP responsive element binding protein-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "cAMP responsive element binding protein-like 1" encoded by a nucleic acid that hybridizes to the "cAMP responsive element binding protein-like 1" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the Pen-2 complex:

1. A protein complex selected from complex (I) and comprising:

(a) at least one first protein selected from the group consisting of:

(i) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(ii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(iii) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and

(iv) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "Alpha-2 catenin" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,

(ii) "Copine III" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,

(iii) "Dachshund 2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(v) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102"

encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,

(vi) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(vii) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(viii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(ix) "TPST1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and

(x) "ZIP kinase" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. The protein complex according to No. 1 wherein the first protein is the protein "Pen-2" (SEQ ID No:15), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "Alpha-2 catenin" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (iii) "Copine III" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (iv) "Dachshund 2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (viii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (ix) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (x) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiii) "TPST1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "ZIP kinase" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 9 of the following proteins:

- (i) "Alpha-2 catenin" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

- (iii) "Copine III" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (iv) "Dachshund 2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (viii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (ix) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (x) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

- (xi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiii) "TPST1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions,
- (xiv) "ZIP kinase" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or

transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Pen-2 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Pen-2 complex selected from

(i) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,

(ii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and

(iii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and

an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,
- (ii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15"

encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,

(ii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or

(iii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, comprising the steps of:

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

(a) exposing said complex, or a cell or organism containing Pen-2 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the

presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "Alpha-2 catenin" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Copine III" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "Dachshund 2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15"

encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "TPST1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "ZIP kinase" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity,

or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether
(i) "Alpha-2 catenin" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Copine III" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Dachshund 2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dachshund

2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or

(v) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or

(vi) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions, and/or

(vii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(x) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or

(xi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(xii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or

- (xiii) "TPST1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "ZIP kinase" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

- (i) "Alpha-2 catenin" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (iii) "Copine III" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (iv) "Dachshund 2" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-1 catenin" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC2803" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (viii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin"

encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(ix) "Pen-2" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(x) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xi) "Presenilin 2" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(xii) "TNRC15" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(xiii) "TPST1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or (xiv) "ZIP kinase" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the APP complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:

- (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
 - (ii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
 - (iii) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
 - (iv) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and
 - (v) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "Bcl-XL-binding protein v68 " (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Bcl-XL-binding protein v68 " encoded by a nucleic acid that hybridizes to the "Bcl-XL-binding protein v68 " nucleic acid or its complement under low stringency conditions,
 - (ii) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
 - (iii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(iv) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and

(v) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. The protein complex according to No. 1 wherein the first protein is the protein "APP" (SEQ ID No:29), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "Bcl-XL-binding protein v68" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Bcl-XL-binding protein v68" encoded by a nucleic acid that hybridizes to the "Bcl-XL-binding protein v68" nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

- (iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (vii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (viii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (ix) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 4 of the following proteins:

- (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a

- nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "Bcl-XL-binding protein v68 " (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Bcl-XL-binding protein v68 " encoded by a nucleic acid that hybridizes to the "Bcl-XL-binding protein v68 " nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (vii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (viii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (ix) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the APP complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the APP complex selected from

(i) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

(a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said

proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, comprising the steps of:

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

- (a) exposing said complex, or a cell or organism containing APP complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription

level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Bcl-XL-binding protein v68 " (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Bcl-XL-binding protein v68 " encoded by a nucleic acid that hybridizes to the "Bcl-XL-binding protein v68 " nucleic acid or its complement under low stringency conditions, and/or

(iii) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a

nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(viii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(ix) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament

for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Bcl-XL-binding protein v68 " (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Bcl-XL-binding protein v68 " encoded by a nucleic acid that hybridizes to the "Bcl-XL-binding protein v68 " nucleic acid or its complement under low stringency conditions, and/or

(iii) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(viii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100

alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(ix) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

- (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "Bcl-XL-binding protein v68 " (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Bcl-XL-binding protein v68 " encoded by a nucleic acid that hybridizes to the "Bcl-XL-binding protein v68 " nucleic acid or its complement under low stringency conditions,
- (iii) "FLJ10773" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (vii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(viii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(ix) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or(x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the APP695SW complex:

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

(ii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iii) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

- (iv) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and
- (v) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions,
- (ii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and
- (iii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

2. The protein complex according to No. 1 wherein the first protein is the protein "APP695SW" (SEQ ID No:232), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW"

encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (vii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(viii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions,

(iii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iv) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(v) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(vi) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(vii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (III) and comprising the following proteins:

- (i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof,
- (ii) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof,
- (iii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof,
- (iv) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof,
- (v) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof,
- (vi) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, and
- (vii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof,

4. The protein complex according to No. 1 comprising all but 1 - 2 of the following proteins:

- (i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (vii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (viii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or

several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the APP695SW complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the APP695SW complex selected from

(i) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:
- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
- (i) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:
- (i) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions, comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.
26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing APP695SW complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or

(ii) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions, and/or

- (iii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

(i) "APP695SW" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

- (ii) "FLJ10773 " (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "FLJ10773 " encoded by a nucleic acid that hybridizes to the "FLJ10773 " nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (vi) "JIP-1" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (vii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or(viii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the APP-C99 complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
 - (ii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
 - (iii) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and
 - (iv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
 - (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
 - (ii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,
 - (iii) "Integral membrane transporter protein" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

- (iv) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,
- (v) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (vi) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (viii) "NAP-1 related protein" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (ix) "Neurocalcin delta" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (x) "REST corepressor" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xi) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and
- (xii) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta"

encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. The protein complex according to No. 1 wherein the first protein is the protein "APP-C99" (SEQ ID No:30), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

- (v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vi) "Integral membrane transporter protein" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (ix) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (x) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xi) "NAP-1 related protein" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xii) "Neurocalcin delta" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,

- (xiii) "REST corepressor" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xiv) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 11 of the following proteins:

- (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a

nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(vi) "Integral membrane transporter protein" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(vii) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(ix) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,

(x) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xi) "NAP-1 related protein" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,

(xii) "Neurocalcin delta" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurocalcin

delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,

(xiii) "REST corepressor" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

(xiv) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xv) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xvi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several

interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the APP-C99 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the APP-C99 complex selected from

(i) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,

(ii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949"

encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(iii) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and

(iv) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or

functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,

- (ii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442"

encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, comprising the steps of:

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

- (a) exposing said complex, or a cell or organism containing APP-C99 complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Integral membrane transporter protein" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(vii) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (x) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "NAP-1 related protein" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Neurocalcin delta" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "REST corepressor" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions; and/or
- (xv) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta"

encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Integral membrane transporter protein" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that

hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(vii) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions, and/or

(viii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or

(ix) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

(x) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xi) "NAP-1 related protein" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Neurocalcin delta" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "REST corepressor" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xv) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

- (i) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65L1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vi) "Integral membrane transporter protein" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1102" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1102" encoded by a nucleic acid that hybridizes to the "KIAA1102" nucleic acid or its complement under low stringency conditions,

- (viii) "KIAA1949" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (ix) "MGC4022" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (x) "MGC5442" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xi) "NAP-1 related protein" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xii) "Neurocalcin delta" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiii) "REST corepressor" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xiv) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 beta" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or (xvi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to

the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the Tau complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
 - (ii) "Actin" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
 - (iii) "Alpha tubulin" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
 - (iv) "Beta tubulin" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
 - (v) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,
 - (vi) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that

hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(vii) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(viii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and

(ix) "Tau" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "Deoxyhypusine synthase " (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Deoxyhypusine synthase " encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase " nucleic acid or its complement under low stringency conditions,

(ii) "Dynactin 2 " (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynactin 2 " encoded by a nucleic acid that hybridizes to the "Dynactin 2 " nucleic acid or its complement under low stringency conditions,

(iii) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,

(iv) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and

(v) "S-100 beta " (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta " encoded by a nucleic acid that hybridizes to the "S-100 beta " nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

2. The protein complex according to No. 1 wherein the first protein is the protein "Tau" (SEQ ID No:250), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha

tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,

(iv) "Beta tubulin" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,

(v) "Deoxyhypusine synthase " (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Deoxyhypusine synthase " encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase " nucleic acid or its complement under low stringency conditions,

(vi) "Dynactin 2 " (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynactin 2 " encoded by a nucleic acid that hybridizes to the "Dynactin 2 " nucleic acid or its complement under low stringency conditions,

(vii) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,

(viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that

hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta " (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta " encoded by a nucleic acid that hybridizes to the "S-100 beta " nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Tau" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 4 of the following proteins:

(i) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,

(ii) "Actin" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,

- (iii) "Alpha tubulin" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase " (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Deoxyhypusine synthase " encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase " nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2 " (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynactin 2 " encoded by a nucleic acid that hybridizes to the "Dynactin 2 " nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,
- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta " (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta " encoded by a nucleic acid that hybridizes to the "S-100 beta " nucleic acid or its complement under low stringency conditions,

(xiv) "Tau" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Tau complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Tau complex selected from

(i) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X

SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
- (i) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.
24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:
- (i) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

(a) exposing said complex, or a cell or organism containing Tau complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3

protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Actin" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Alpha tubulin" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Beta tubulin" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or

(v) "Deoxyhypusine synthase " (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Deoxyhypusine synthase " encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase " nucleic acid or its complement under low stringency conditions, and/or

(vi) "Dynactin 2 " (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynactin 2 " encoded by a nucleic acid that hybridizes to the "Dynactin 2 " nucleic acid or its complement under low stringency conditions, and/or

(vii) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or

- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "S-100 beta " (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta " encoded by a nucleic acid that hybridizes to the "S-100 beta " nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Tau" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Actin" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Alpha tubulin" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Beta tubulin" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or

(v) "Deoxyhypusine synthase " (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Deoxyhypusine synthase " encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase " nucleic acid or its complement under low stringency conditions, and/or

(vi) "Dynactin 2 " (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynactin 2 " encoded by a nucleic acid that hybridizes to the "Dynactin 2 " nucleic acid or its complement under low stringency conditions, and/or

(vii) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "S-100 beta " (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta " encoded by a nucleic acid that hybridizes to the "S-100 beta " nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Tau" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Tau" encoded by a

nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:
(i) "14-3-3 protein zeta/delta" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
(ii) "Actin" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,

- (iii) "Alpha tubulin" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase " (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Deoxyhypusine synthase " encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase " nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2 " (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Dynactin 2 " encoded by a nucleic acid that hybridizes to the "Dynactin 2 " nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,
- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta " (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 beta " encoded by a nucleic acid that hybridizes to the "S-100 beta " nucleic acid or its complement under low stringency conditions, and/or(xiv) "Tau" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the BACE1 D215N complex:

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "BACE1 D215N" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1

D215N" encoded by a nucleic acid that hybridizes to the "BACE1 D215N" nucleic acid or its complement under low stringency conditions, and

(ii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "ADP-ribosylation factor 4" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 4" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 4" nucleic acid or its complement under low stringency conditions,

(ii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iii) "Acetylcholine receptor beta-4" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetylcholine receptor beta-4" encoded by a nucleic acid that hybridizes to the "Acetylcholine receptor beta-4" nucleic acid or its complement under low stringency conditions,

(iv) "Calcium binding protein Cab45" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium binding protein Cab45" encoded by a nucleic acid that hybridizes to the "Calcium binding protein Cab45" nucleic acid or its complement under low stringency conditions,

(v) "DNAJC3" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,

(vi) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,

- (vii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0747" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0747" encoded by a nucleic acid that hybridizes to the "KIAA0747" nucleic acid or its complement under low stringency conditions,
- (ix) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (x) "Neural cell adhesion molecule L1 " (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,
- (xi) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,
- (xiii) "Protocadherin beta 10" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 10" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 10" nucleic acid or its complement under low stringency conditions,
- (xiv) "Protocadherin beta 14" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 14" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 14" nucleic acid or its complement under low stringency conditions,

(xv) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions,

(xvi) "Protocadherin gamma C3" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,

(xvii) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xviii) "SEL-1 homologue" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SEL-1 homologue" encoded by a nucleic acid that hybridizes to the "SEL-1 homologue" nucleic acid or its complement under low stringency conditions,

(xix) "Seipin" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Seipin" encoded by a nucleic acid that hybridizes to the "Seipin" nucleic acid or its complement under low stringency conditions, and

(xx) "Stromal cell-derived factor 2-like 1" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. The protein complex according to No. 1 wherein the first protein is the protein "BACE1 D215N" (SEQ ID No:266), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1 D215N" encoded by a nucleic acid that hybridizes to the "BACE1 D215N" under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

(i) "ADP-ribosylation factor 4" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 4" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 4" nucleic acid or its complement under low stringency conditions,

(ii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iii) "Acetylcholine receptor beta-4" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetylcholine receptor beta-4" encoded by a nucleic acid that hybridizes to the "Acetylcholine receptor beta-4" nucleic acid or its complement under low stringency conditions,

(iv) "BACE1 D215N" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1 D215N" encoded by a nucleic acid that hybridizes to the "BACE1 D215N" nucleic acid or its complement under low stringency conditions,

(v) "Calcium binding protein Cab45" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium binding protein Cab45" encoded by a nucleic acid that hybridizes to the "Calcium binding protein Cab45" nucleic acid or its complement under low stringency conditions,

(vi) "DNAJC3" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,

- (vii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,
- (viii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA0747" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0747" encoded by a nucleic acid that hybridizes to the "KIAA0747" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xi) "Neural cell adhesion molecule L1 " (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,
- (xii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xv) "Protocadherin beta 10" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 10" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 10" nucleic acid or its complement under low stringency conditions,

(xvi) "Protocadherin beta 14" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 14" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 14" nucleic acid or its complement under low stringency conditions,

(xvii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions,

(xviii) "Protocadherin gamma C3" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,

(xix) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xx) "SEL-1 homologue" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SEL-1 homologue" encoded by a nucleic acid that hybridizes to the "SEL-1 homologue" nucleic acid or its complement under low stringency conditions,

(xxi) "Seipin" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Seipin" encoded by a nucleic acid that hybridizes to the "Seipin" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 19 of the following proteins:

(i) "ADP-ribosylation factor 4" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 4" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 4" nucleic acid or its complement under low stringency conditions,

(ii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iii) "Acetylcholine receptor beta-4" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetylcholine receptor beta-4" encoded by a nucleic acid that hybridizes to the "Acetylcholine receptor beta-4" nucleic acid or its complement under low stringency conditions,

(iv) "BACE1 D215N" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1 D215N" encoded by a nucleic acid that hybridizes to the "BACE1 D215N" nucleic acid or its complement under low stringency conditions,

(v) "Calcium binding protein Cab45" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium binding protein Cab45" encoded by a nucleic acid that hybridizes to the "Calcium binding protein Cab45" nucleic acid or its complement under low stringency conditions,

(vi) "DNAJC3" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,

(vii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,

- (viii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA0747" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0747" encoded by a nucleic acid that hybridizes to the "KIAA0747" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xi) "Neural cell adhesion molecule L1 " (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,
- (xii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (xiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (xiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,
- (xv) "Protocadherin beta 10" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 10" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 10" nucleic acid or its complement under low stringency conditions,

- (xvi) "Protocadherin beta 14" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 14" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 14" nucleic acid or its complement under low stringency conditions,
- (xvii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions,
- (xviii) "Protocadherin gamma C3" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,
- (xix) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xx) "SEL-1 homologue" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SEL-1 homologue" encoded by a nucleic acid that hybridizes to the "SEL-1 homologue" nucleic acid or its complement under low stringency conditions,
- (xxi) "Seipin" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Seipin" encoded by a nucleic acid that hybridizes to the "Seipin" nucleic acid or its complement under low stringency conditions,
- (xxii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said

second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:

expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the BACE1 D215N complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the BACE1 D215N complex selected from

- (i) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and
- (ii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the

nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248"

encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions, comprising the steps of:

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

(a) exposing said complex, or a cell or organism containing BACE1 D215N complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the

complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "ADP-ribosylation factor 4" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 4" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 4" nucleic acid or its complement under low stringency conditions, and/or (ii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or (iii) "Acetylcholine receptor beta-4" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

- "Acetylcholine receptor beta-4" encoded by a nucleic acid that hybridizes to the "Acetylcholine receptor beta-4" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "BACE1 D215N" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1 D215N" encoded by a nucleic acid that hybridizes to the "BACE1 D215N" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Calcium binding protein Cab45" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium binding protein Cab45" encoded by a nucleic acid that hybridizes to the "Calcium binding protein Cab45" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "DNAJC3" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "KIAA0747" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0747" encoded by a nucleic acid that hybridizes to the "KIAA0747" nucleic acid or its complement under low stringency conditions, and/or
- (x) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Neural cell adhesion molecule L1" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a

variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions, and/or

(xii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Protocadherin beta 10" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 10" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 10" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Protocadherin beta 14" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 14" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 14" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "Protocadherin gamma C3" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions, and/or

- (xix) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "SEL-1 homologue" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SEL-1 homologue" encoded by a nucleic acid that hybridizes to the "SEL-1 homologue" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "Seipin" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Seipin" encoded by a nucleic acid that hybridizes to the "Seipin" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or

disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "ADP-ribosylation factor 4" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 4" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 4" nucleic acid or its complement under low stringency conditions, and/or (ii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Acetylcholine receptor beta-4" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetylcholine receptor beta-4" encoded by a nucleic acid that hybridizes to the "Acetylcholine receptor beta-4" nucleic acid or its complement under low stringency conditions, and/or

(iv) "BACE1 D215N" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1 D215N" encoded by a nucleic acid that hybridizes to the "BACE1 D215N" nucleic acid or its complement under low stringency conditions, and/or

(v) "Calcium binding protein Cab45" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calcium binding protein Cab45" encoded by a nucleic acid that hybridizes to the "Calcium binding protein Cab45" nucleic acid or its complement under low stringency conditions, and/or

(vi) "DNAJC3" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(ix) "KIAA0747" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0747" encoded by a nucleic acid that hybridizes to the "KIAA0747" nucleic acid or its complement under low stringency conditions, and/or

(x) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

- (xi) "Neural cell adhesion molecule L1 " (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 ." nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Protocadherin beta 10" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 10" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 10" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Protocadherin beta 14" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 14" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 14" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Protocadherin gamma C3" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the

"Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions, and/or

(xix) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xx) "SEL-1 homologue" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SEL-1 homologue" encoded by a nucleic acid that hybridizes to the "SEL-1 homologue" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Seipin" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Seipin" encoded by a nucleic acid that hybridizes to the "Seipin" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi

(siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

- (i) "ADP-ribosylation factor 4" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "ADP-ribosylation factor 4" encoded by a nucleic acid that hybridizes to the "ADP-ribosylation factor 4" nucleic acid or its complement under low stringency conditions,
- (ii) "APP" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iii) "Acetylcholine receptor beta-4" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Acetylcholine receptor beta-4" encoded by a nucleic acid that hybridizes to the "Acetylcholine receptor beta-4" nucleic acid or its complement under low stringency conditions,
- (iv) "BACE1 D215N" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "BACE1 D215N" encoded by a nucleic acid that hybridizes to the "BACE1 D215N" nucleic acid or its complement under low stringency conditions,
- (v) "Calcium binding protein Cab45" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of

"Calcium binding protein Cab45" encoded by a nucleic acid that hybridizes to the "Calcium binding protein Cab45" nucleic acid or its complement under low stringency conditions,

(vi) "DNAJC3" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "DNAJC3" encoded by a nucleic acid that hybridizes to the "DNAJC3" nucleic acid or its complement under low stringency conditions,

(vii) "Delta-like homologue" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Delta-like homologue" encoded by a nucleic acid that hybridizes to the "Delta-like homologue" nucleic acid or its complement under low stringency conditions,

(viii) "Fe65" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA0747" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KIAA0747" encoded by a nucleic acid that hybridizes to the "KIAA0747" nucleic acid or its complement under low stringency conditions,

(x) "MGC4248" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xi) "Neural cell adhesion molecule L1 " (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neural cell adhesion molecule L1 " encoded by a nucleic acid that hybridizes to the "Neural cell adhesion molecule L1 " nucleic acid or its complement under low stringency conditions,

(xii) "Neurotrypsin" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xiii) "Nicastrin" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Nicastrin"

encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xv) "Protocadherin beta 10" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 10" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 10" nucleic acid or its complement under low stringency conditions,

(xvi) "Protocadherin beta 14" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 14" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 14" nucleic acid or its complement under low stringency conditions,

(xvii) "Protocadherin beta 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin beta 7" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 7" nucleic acid or its complement under low stringency conditions,

(xviii) "Protocadherin gamma C3" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Protocadherin gamma C3" encoded by a nucleic acid that hybridizes to the "Protocadherin gamma C3" nucleic acid or its complement under low stringency conditions,

(xix) "S-100 alpha" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xx) "SEL-1 homologue" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "SEL-1 homologue" encoded by a nucleic acid that hybridizes to the "SEL-1 homologue" nucleic acid or its complement under low stringency conditions,

(xxi) "Seipin" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Seipin" encoded by a

nucleic acid that hybridizes to the "Seipin" nucleic acid or its complement under low stringency conditions, and/or (xxii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the Calsenilin complex:

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein selected from the group consisting of:
 - (i) "Calsenilin" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsenilin" encoded by a nucleic acid that hybridizes to the "Calsenilin" nucleic acid or its complement under low stringency conditions, and
 - (ii) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
 - (i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions,
 - (ii) "KCNQ2" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KCNQ2" encoded by a nucleic acid that hybridizes to the "KCNQ2" nucleic acid or its complement under low stringency conditions, and

(iii) "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" encoded by a nucleic acid that hybridizes to the "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C , washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C , and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C .

2. The protein complex according to No. 1 wherein the first protein is the protein "Calsenilin" (SEQ ID No:263), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsenilin" encoded by a nucleic acid that hybridizes to the "Calsenilin" under low stringency conditions.

3. The protein complex according to No. 1 comprising the following proteins:

(i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions,

(ii) "Calsenilin" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsenilin" encoded by a nucleic acid that hybridizes to the "Calsenilin" nucleic acid or its complement under low stringency conditions,

(iii) "KCNQ2" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KCNQ2" encoded by a nucleic acid that hybridizes to the "KCNQ2" nucleic acid or its complement under low stringency conditions,

(iv) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1"

encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or

(v) "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" encoded by a nucleic acid that hybridizes to the "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 2 of the following proteins:

(i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions,

(ii) "Calsenilin" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsenilin" encoded by a nucleic acid that hybridizes to the "Calsenilin" nucleic acid or its complement under low stringency conditions,

(iii) "KCNQ2" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KCNQ2" encoded by a nucleic acid that hybridizes to the "KCNQ2" nucleic acid or its complement under low stringency conditions,

(iv) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(v) "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" encoded by a nucleic acid that hybridizes to the "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the activation of Calsenilin target genes including prodynorphin that contain DRE elements (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the activation or inactivation of potassium channels by compounds (e.g. Retigabine) and their effect on transcriptional processes regulated directly or indirectly by Calsenilin.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:
expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Calsenilin complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Calsenilin complex selected from

(i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising:

- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions; comprising the steps of:

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of:

(a) exposing said complex, or a cell or organism containing Calsenilin complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said

isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Calsenilin" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsenilin" encoded by a nucleic acid that hybridizes to the "Calsenilin" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "KCNQ2" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KCNQ2" encoded by a nucleic acid that hybridizes to the "KCNQ2" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" encoded by a nucleic acid that hybridizes to the "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Calsenilin" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsenilin" encoded by a nucleic acid that hybridizes to the "Calsenilin" nucleic acid or its complement under low stringency conditions, and/or

(iii) "KCNQ2" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KCNQ2" encoded by a nucleic acid that hybridizes to the "KCNQ2" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or

(v) "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" encoded by a nucleic acid that hybridizes to the "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the activation of Calsenilin target genes including prodynorphin that contain DRE elements (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the activation or inactivation of potassium channels by compounds (e.g. Retigabine) and their effect on transcriptional processes regulated directly or indirectly by Calsenilin, or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins:

(i) "C21ORF57" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "C21ORF57" encoded by a nucleic acid that hybridizes to the "C21ORF57" nucleic acid or its complement under low stringency conditions,

(ii) "Calsenilin" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Calsenilin" encoded by a nucleic acid that hybridizes to the "Calsenilin" nucleic acid or its complement under low stringency conditions,

(iii) "KCNQ2" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "KCNQ2" encoded by a nucleic acid that hybridizes to the "KCNQ2" nucleic acid or its complement under low stringency conditions,

(iv) "Presenilin 1" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or(v) "UDP-GalNAc:polypeptide N-

acetylgalactosaminyltransferase 7" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" encoded by a nucleic acid that hybridizes to the "UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

5. PROTOCOLS:

The TAP-technology, which is more fully described in EP 1 105 508 B1 and in Rigaut, et al., 1999, Nature Biotechnol. 17:1030-1032 respectively was used and further adapted as described below for protein purification. Proteins were identified using mass spectrometry as described further below.

5.1 Construction of TAP-tagged bait

The cDNAs encoding the complete ORF were obtained by RT-PCR. Total RNA was prepared from appropriate cell lines using the RNeasy Mini Kit (Qiagen). Both cDNA synthesis and PCR were performed with the SUPERScript One-Step RT-PCR for Long templates Kit (Life Technologies) using gene-specific primers. After 35-40 cycles of amplification PCR-products with the expected size were gel-purified with the MinElute PCR Purification Kit (Qiagen) and, if necessary, used for further amplification. Low-abundant RNAs were amplified by nested PCR before gel-purification. Restriction sites for NotI were attached to PCR primers to allow subcloning of amplified cDNAs into the retroviral vectors pIE94-N/C-TAP thereby generating N- or C-terminal fusions with the TAP-tag (Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032). N-terminal tagging was chosen for the following baits/entry points: Presenilin 1, Presenilin 2, Aph-1a, Aph-1b, Pen-2, APP, Tau, Fe65, Calsenilin. C-terminal tagging was chosen for the following baits/entry points: Nicastrin, Aph-1a, Aph-1b, BACE1 D215N, APP, APP695SW, APP-C99, Fe65, X11beta.

Clones were analyzed by restriction digest, DNA sequencing and by in vitro translation using the TNT T7 Quick Coupled Transcription/Translation System (Promega inc.). The presence of the proteins was proven by Western blotting using the protein A part of the TAP-tag for detection. Briefly, separation of proteins by standard SDS-PAGE was followed by semi-dry transfer onto a nitrocellulose membrane (PROTRAN, Schleicher&Schuell) using the MultiphorII blotting apparatus from Pharmacia Biotech. The transfer buffer consisted of 48 mM Tris, 39 mM glycine, 10% methanol and 0,0375% sodium dodecylsulfate. After blocking in phosphate-buffered saline (PBS) supplemented with 10% dry milk powder and 0,1% Tween 20 transferred proteins were probed with the Peroxidase-Anti-Peroxidase Soluble Complex (Sigma) diluted in blocking solution. After intensive washing immunoreactive proteins were visualized by enhanced chemiluminescence (ECL; Amersham Pharmacia Biotech).

5.2 Preparation of Virus and infection

As a vector, a MoMLV-based recombinant virus was used.

The preparation has been carried out as follows:

5.2.1 Preparation of Virus

293 gp cells were grown to 100% confluency. They were split 1:5 on poly-L-Lysine plates (1:5 diluted poly-L-Lysine [0.01% stock solution, Sigma P-4832] in PBS, left on plates for at least 10 min.). On Day 2, 63 microgram of retroviral Vector DNA together with 13 microgram of DNA of plasmid encoding an appropriate envelope protein were transfected into 293 gp cells (Somia, et al., 1999, Proc. Natl. Acad. Sci. USA 96:12667-12672; Somia, et al. 2000, J. Virol. 74:4420-4424). On Day 3, the medium was replaced with 15 ml DMEM + 10% FBS per 15-cm dish. On Day 4, the medium containing viruses (supernatant) was harvested (at 24 h following medium change after transfection). When a second collection was planned, DMEM 10 % FBS was added to the plates and the plates were incubated for another 24 h. All collections were done as follows: The supernatant was filtered through 0.45 micrometer filter (Corning GmbH, cellulose acetate, 431155). The filter was placed into konical polyallomer centrifuge tubes

(Beckman, 358126) that are placed in buckets of a SW 28 rotor (Beckman). The filtered supernatant was ultracentrifuged at 19400 rpm in the SW 28 rotor, for 2 hours at 21 degree Celsius. The supernatant was discarded. The pellet containing viruses was resuspended in a small volume (for example 300 microliter) of Hank's Balanced Salt Solution [Gibco BRL, 14025-092], by pipetting up and down 100-times, using an aerosol-safe tip. The viruses were used for transfection as described below.

5.2.2 Infection

Cells that were infected were plated one day before into one well of a 6-well plate. 4 hours before infection, the old medium on the cells was replaced with fresh medium. Only a minimal volume was added, so that the cells are completely covered (e.g. 700 microliter). During infection, the cells were actively dividing.

A description of the cells and their growth conditions is given in 5.2.3

To the concentrated virus, polybrene (Hexadimethrine Bromide; Sigma, H 9268) was added to achieve a final concentration of 8 microgram/ml (this is equivalent to 2.4 microliter of the 1 milligram/ml polybrene stock per 300 microliter of concentrated retrovirus). The virus was incubated in polybrene at room temperature for 1 hour. For infection, the virus/polybrene mixture was added to the cells and incubated at 37 degree Celsius at the appropriate CO₂ concentration for several hours (e.g. over-day or over-night). Following infection, the medium on the infected cells was replaced with fresh medium. The cells were passaged as usual after they became confluent. The cells contain the retrovirus integrated into their chromosomes and stably express the gene of interest.

5.2.3 Cell lines

For expression, SKN-BE2 cells were used. SKN-BE2 cells (American Type Culture Collection-No. CRL-2271) were grown in 95% OptiMEM + 5% iron-supplemented calf serum.

The expression pattern of the TAP-tagged proteins was checked by immunoblot-analysis as described in 5.3.3 and/or by immunofluorescence as described in 5.3.1 or 5.3.2.

5.3 Checking of expression pattern of TAP-tagged proteins

The expression pattern of the TAP-tagged protein was checked by immunoblot analysis and/or by immunofluorescence. Immunofluorescence analysis was either carried out according to section 5.3.1 or to section 5.3.2 depending on the type of the TAP-tagged protein. Immunoblot analysis was carried out according to section 5.3.3.

5.3.1 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for plasma membrane and ER bound proteins

Cells were grown in FCS media on polylysine coated 8 well chamber slides to 50% confluency. Then fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4). The cells were incubated for 30 minutes at room temperature in 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Blocking was performed with 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at room temperature. Incubation of the primary antibodies was performed in the blocking solution overnight at +4°C. The proper dilution of the antibodies was determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin for 2x 20 minutes at room temperature. Incubation of the secondary antibodies is performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes). Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin was used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were then washed again 2x 20 minutes at room temperature in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

5.3.2 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for non-plasma membrane bound proteins:

Cells were grown in FCS media on Polylysine coated 8 well chamber slides to 50% confluency. Fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4) for 30 minutes at Room Temperature (RT), 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Permeabilization of cells was done with 0.5% Triton X-100 in PBS for 10 minutes at room temperature. Blocking was then done in 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at RT (Blocking solution). Incubation of the primary antibodies was performed in the blocking solution, overnight at +4°C. The proper dilution of the antibodies has to be determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin, for 2x 20 minutes at RT. Incubation of the secondary antibodies was performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes), Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin is used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were washed 2x 20 minutes at RT in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

5.3.3 Immunoblot analysis

To analyze expression levels of TAP-tagged proteins, a cell pellet (from a 6-well dish) was lysed in 60 μ l DNase I buffer (5% Glycerol, 100 mM NaCl, 0.8 % NP-40 (IGEPAL), 5 mM magnesium sulfate, 100 μ g/ml DNase I (Roche Diagnostics), 50 mM Tris, pH 7.5, protease inhibitor cocktail) for 15 min on ice. Each sample was split into two aliquots. The first half was centrifuged at 13,000 rpm for 5 min. to yield the NP-40-extractable material in the supernatant; the second half (total material) was carefully triturated. 50 μ g each of the NP-40-extractable material and the total material are mixed with DTT-containing sample buffer for 30 min at 50°C on a shaker and separated by SDS

polyacrylamide gel electrophoresis on a precast 4-12% Bis-Tris gel (Invitrogen). Proteins were then transferred to nitrocellulose using a semi-dry procedure with a discontinuous buffer system. Briefly, gel and nitrocellulose membrane were stacked between filter papers soaked in either anode buffer (three layers buffer A1 (0.3 M Tris-HCl) and three layers buffer A2 (0.03 M Tris-HCl)) or cathode buffer (three layers of 0.03 M Tris-HCl, pH 9.4, 0.1 % SDS, 40 mM ϵ -aminocaproic acid). Electrotransfer of two gels at once was performed at 600 mA for 25 min. Transferred proteins were visualized with Ponceau S solution for one min to control transfer efficiency and then destained in water. The membrane was blocked in 5% non-fat milk powder in TBST (TBS containing 0.05% Tween-20) for 30 min at room temperature. It was subsequently incubated with HRP-coupled PAP antibody (1:5000 diluted in 5% milk/TBST) for 1 h at room temperature, washed three times for 10 min in TBST. The blot membrane was finally soaked in chemiluminescent substrate (ECL, Roche Diagnostics) for 2 min. and either exposed to X-ray film or analyzed on an imaging station.

5.4 Purification of protein complexes

Protein complex purification was adapted to the sub-cellular localization of the TAP-tagged protein and was performed as described below.

5.4.1 Lysate preparation for cytoplasmic proteins

About 1×10^9 adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of CZ lysis buffer (50 mM Tris-Cl, pH 7.4; 5 % Glycerol; 0,2 % IGEPAL; 1.5 mM $MgCl_2$; 100 mM NaCl; 25 mM NaF; 1 mM Na_3VO_4 ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was incubated for 30 min on ice and spun for 10 min at 20,000g. The supernatant was subjected to an additional ultracentrifugation step for 1 h at 100,000g. The supernatant was recovered and rapidly frozen in liquid nitrogen or immediately processed further.

5.4.2 Lysate preparation for membrane proteins

About 1×10^9 adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Membrane-Lysis buffer (50 mM Tris, pH 7.4; 7.5 % Glycerol; 1 mM EDTA; 150 mM NaCl; 25 mM NaF; 1 mM Na_3VO_4 ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 750g, the supernatant was recovered and subjected to an ultracentrifugation step for 1 h at 100,000g. The membrane pellet was resuspended in 7,5 ml of Membrane-Lysis buffer containing 0.8% n-Dodecyl- β -D-maltoside and incubated for 1 h at 4°C with constant agitation. The sample was subjected to another ultracentrifugation step for 1h at 100,000g and the solubilized material was quickly frozen in liquid nitrogen or immediately processed further.

5.4.3 Lysate preparation for nuclear proteins

About 1×10^9 adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Hypotonic-Lysis buffer (10 mM Tris, pH 7.4; 1.5 mM MgCl_2 ; 10 mM KCl; 25 mM NaF; 1 mM Na_3VO_4 ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 2,000g and the resulting supernatant (S1) saved on ice. The nuclear pellet (P1) was resuspended in 5 ml Nuclear-Lysis buffer (50 mM Tris, pH 7.4; 1.5 mM MgCl_2 ; 20 % Glycerol; 420 mM NaCl; 25 mM NaF; 1 mM Na_3VO_4 ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and incubated for 30 min on ice. The sample was combined with S1, further diluted with 7 ml of Dilution buffer (110 mM Tris, pH 7.4; 0.7 % NP40; 1.5 mM MgCl_2 ; 25 mM NaF; 1 mM

Na₃VO₄; 1 mM DTT), incubated on ice for 10 min and centrifuged at 100,000g for 1h. The final supernatant (S2) was frozen quickly in liquid nitrogen.

5.4.4 Tandem Affinity Purification

The frozen lysate was quickly thawed in a 37°C water bath, and spun for 20 min at 100,000g. The supernatant was recovered and incubated with 0.2 ml of settled rabbit IgG-Agarose beads (Sigma) for 2 h with constant agitation at 4°C. Immobilized protein complexes were washed with 10 ml of CZ lysis buffer (containing 1 Complete™ tablet (Roche) per 50 ml of buffer) and further washed with 5 ml of TEV cleavage buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 0.5 mM EDTA; 1 mM DTT). Protein-complexes were eluted by incubation with 5 µl of TEV protease (GibcoBRL, Cat.No. 10127-017) for 1 h at 16°C in 150 µl TEV cleavage buffer. The eluate was recovered and combined with 0.2 ml settled Calmodulin affinity beads (Stratagene) in 0.2 ml CBP binding buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 2mM MgAc; 2mM Imidazole; 1mM DTT; 4 mM CaCl₂) followed by 1 h incubation at 4°C with constant agitation. Immobilized protein complexes were washed with 10 ml of CBP wash buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 1mM MgAc; 1mM Imidazole; 1mM DTT; 2 mM CaCl₂) and eluted by addition of 600 µl CBP elution buffer (10 mM Tris, pH 8.0; 5 mM EGTA) for 5 min at 37°C. The eluate was recovered in a siliconized tube and lyophilized. The remaining Calmodulin resin was boiled for 5 min in 50 µl 4x Laemmli sample buffer. The sample buffer was isolated, combined with the lyophilised fraction and loaded on a NuPAGE gradient gel (Invitrogen, 4-12%, 1.5 mm, 10 well).

5.5 Protein Identification by Mass Spectrometry

5.5.1 Protein digestion prior to mass spectrometric analysis

Gel-separated proteins were reduced, alkylated and digested in gel essentially following the procedure described by Shevchenko et al., 1996, Anal. Chem. 68:850-858. Briefly, gel-separated proteins were excised from the gel using a clean scalpel, reduced using 10 mM DTT (in 5mM ammonium bicarbonate, 54°C, 45 min) and subsequently

alkylated with 55 mM iodoacetamid (in 5 mM ammonium bicarbonate) at room temperature in the dark (30 min). Reduced and alkylated proteins were digested in gel with porcine trypsin (Promega) at a protease concentration of 12.5 ng/ μ l in 5mM ammonium bicarbonate. Digestion was allowed to proceed for 4 hours at 37°C and the reaction was subsequently stopped using 5 μ l 5% formic acid.

5.5.2 Sample preparation prior to analysis by mass spectrometry

Gel plugs were extracted twice with 20 μ l 1% TFA and pooled with acidified digest supernatants. Samples were dried in a vacuum centrifuge and resuspended in 13 μ l 1% TFA.

5.5.3 Mass spectrometric data acquisition

Peptide samples were injected into a nano LC system (CapLC, Waters or Ultimate, Dionex) which was directly coupled either to a quadrupole TOF (QTOF2, QTOF Ultima, QTOF Micro, Micromass or QSTAR Pulsar, Sciex) or ion trap (LCQ Deca XP) mass spectrometer. Peptides were separated on the LC system using a gradient of aqueous and organic solvents (see below). Solvent A was 5% acetonitrile in 0.5% formic acid and solvent B was 70% acetonitrile in 0.5% formic acid.

Time (min)	% solvent A	% solvent B
0	95	5
5.33	92	8
35	50	50
36	20	80
40	20	80
41	95	5
50	95	5

Peptides eluting off the LC system were partially sequenced within the mass spectrometer.

5.5.4 Protein identification

The peptide mass and fragmentation data generated in the LC-MS/MS experiments were used to query fasta formatted protein and nucleotide sequence databases maintained and updated regularly at the NCBI (for the NCBI nr, dbEST and the human and mouse genomes) and European Bioinformatics Institute (EBI, for the human, mouse, *D. melanogaster* and *C. elegans* proteome databases). Proteins were identified by correlating the measured peptide mass and fragmentation data with the same data computed from the entries in the database using the software tool Mascot (Matrix Science; Perkins et al., 1999, *Electrophoresis* 20:3551-3567). Search criteria varied depending on which mass spectrometer was used for the analysis.

TABLE 1

COMPONENTS OF COMPLEXES

Name of complex	Entry Point	All interactors of the complex	Known interactors of the complex	Novel interactors of the complex	Proteins of unknown function
Presenilin 1 complex	Presenilin 1	Alpha catenin	Alpha catenin	BAX inhibitor 1	CGI-147
		Aph-1a	Aph-1a	Cadherin-11 precursor	FKRP
		BAX inhibitor 1	Beta catenin	Cadherin-4 precursor	FLJ20627
		Beta catenin	Delta-2 catenin	CGI-147	MGC5442
		Cadherin-11 precursor	Gamma catenin	FKRP	Sterile alpha and HEAT/Armadillo motif protein
		Cadherin-4 precursor	Nicastrin	MGC5442	
		CGI-147	Delta-1 catenin	Sterile alpha and HEAT/Armadillo motif protein	
		Delta-2 catenin	Pen-2	Sortilin 1	
		FKRP	Plakophilin 4		
		FLJ20627	Presenilin 1		
		Gamma catenin	Ubiquilin		

		MGC5442				
		Nicastrin				
		Delta-1 catenin				
		Pen-2				
		Plakophilin 4				
		Presenilin 1				
		Sortilin 1				
		Sterile alpha and HEAT/Armadillo motif protein				
		Ubiquilin				
Presenilin 2 complex	Presenilin 2	18 kDa microsomal signal peptidase subunit	DOCK3	18 kDa microsomal signal peptidase subunit	Cerebral protein-10	
		200 kDa proteasome activator	Nicastrin	200 kDa proteasome activator	CGI-51	
		Acetolactate synthase	Presenilin 2	Acetolactate synthase	DKFZp586c1924	
		ADP-ribosylation factor 3		ADP-ribosylation factor 3	FLJ20342	
		Adrenoleukodystrophy protein		Adrenoleukodystrophy protein	FLJ20420	

		ATP-binding cassette protein, sub-family B, member 1		ATP-binding cassette protein, sub-family B, member 1	FLJ22555
		ATP-dependent metalloprotease FtsH1 homologue		ATP-dependent metalloprotease FtsH1 homologue	FLJ22678
		Calcium-binding protein P22		Calcium-binding protein P22	KIAA0062
		Cation-chloride cotransporter- interacting protein		Cation-chloride cotransporter- interacting protein	KIAA0090
		Centromere/kinetochor e protein ZW10 homologue		Centromere/kinetoch re protein ZW10 homologue	KIAA0103
		Cerebral protein-10		Cerebral protein-10	KIAA1499
		CGI-51		CGI-51	MGC4248
		DKFZp586c1924		DKFZp586c1924	NICE-3
		DOCK3		Down syndrome critical region protein 2	
		Down syndrome critical region protein 2		ECSIT	
		ECSIT		FLJ20342	

	FLJ20342		FLJ20420	
	FLJ20420		FLJ22555	
	FLJ22555		FLJ22678	
	FLJ22678		Galactosylgalactosylxy losylprotein 3-beta- glucuronosyltransferas e 3	
	Galactosylgalactosylxy osylprotein 3-beta- glucuronosyltransferas e 3		HTRA2	
	HTRA2		HU-K4	
	HU-K4		KIAA0062	
	KIAA0062		KIAA0090	
	KIAA0090		KIAA0103	
	KIAA0103		KIAA1499	
	KIAA1499		MGC4248	
	MGC4248		NICE-3	
	Nicestrin		NPD002	
	NICE-3		P63 protein	
	NPD002		Prohibitin	

	P63 protein		Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3	
	Presenilin 2		PSMA1	
	Prohibitin		PSMA3	
	Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3		PSMA4	
	PSMA1		PSMA6	
	PSMA3		PSMB1	
	PSMA4		PSMB2	
	PSMA6		PSMB3	
	PSMB1		PSMB4	
	PSMB2		PSMB5	
	PSMB3		PSMB6	
	PSMB4		PSMC1	
	PSMB5		PSMC2	
	PSMB6		PSMC3	
	PSMC1		PSMC4	
	PSMC2		PSMC5	

	PSMC3		PSMC6	
	PSMC4		PSMD1	
	PSMC5		PSMD11	
	PSMC6		PSMD12	
	PSMD1		PSMD13	
	PSMD11		PSMD2	
	PSMD12		PSMD3	
	PSMD13		PSMD4	
	PSMD2		Serine/threonine protein phosphatase 6	
	PSMD3		Sortilin 1	
	PSMD4		Stearoyl-CoA desaturase	
	Serine/threonine protein phosphatase 6		Ubiquitin-protein ligase EDD	
	Sortilin 1		Voltage-dependent anion channel 2	
	Stearoyl-CoA desaturase		Wolfgramin	
	Ubiquitin-protein ligase EDD			

		Voltage-dependent anion channel 2				
		Wolframin				
Nicastrin complex	Nicastrin	18 kDa microsomal signal peptidase subunit	Aph-1a	18 kDa microsomal signal peptidase subunit	ATP-binding cassette, sub-family A, member 3	
		25 kDa microsomal signal peptidase subunit	BACE1	25 kDa microsomal signal peptidase subunit	CGI-13	
		Aph-1a	Nicastrin	ATP-binding cassette, sub-family A, member 3	ENSG00000144840	
		ATP-binding cassette, sub-family A member 3	Pen-2	BSCv protein	FLJ20342	
		BACE1	Presenilin-1	Casein kinase II beta chain	FLJ20481	
		BSCv protein	Presenilin-2	Cathepsin B	FLJ22390	
		Casein kinase II beta chain		CGI-13	Hypothetical protein tyrosine phosphatase ensg00000149185	

	Cathepsin B			Delta-6 fatty acid desaturase	KIAA1181
	CGI-13			ENSG00000144840	KIAA1533
	Delta-6 fatty acid desaturase			FLJ13977	PP1, regulatory subunit 15B
	ENSG00000144840			FLJ20342	RING finger protein 5
	FLJ13977			FLJ20481	Thioredoxin domain-containing protein
	FLJ20342			FLJ22390	
	FLJ20481			Hypothetical protein tyrosine phosphatase ensg00000149185	
	FLJ22390			ICAM-2	
	Hypothetical protein tyrosine phosphatase ensg00000149185			KIAA1181	
	ICAM-2			KIAA1533	
	KIAA1181			Mesenchymal stem cell protein DSCD75	
	KIAA1533			Neurotrypsin	

		Mesenchymal stem cell protein DSCD75		NICE-3	
		Neurotrypsin		Protein amplified in osteosarcoma (OS-9)	
		Nicastrin		PP1, regulatory subunit 15B	
		NICE-3		Protein similar to stromal cell-derived factor 2	
		Pen-2		Protocadherin beta 8	
		Presenilin-1		REP8 protein	
		Presenilin-2		Retinal short-chain dehydrogenase/reductase retSDR2	
		Protein amplified in osteosarcoma (OS-9)		RING finger protein 5	
		PP1, regulatory subunit 15B		Stromal cell-derived factor 2-like 1	
		Protein similar to stromal cell-derived factor 2		Thioredoxin domain-containing protein	

		Protocadherin beta 8		Voltage-dependent anion channel 1	
		REP8 protein			
		Retinal short-chain dehydrogenase/reductase retSDR2			
		RING finger protein 5			
		Stromal cell-derived factor 2-like 1			
		Thioredoxin domain-containing protein			
		Voltage-dependent anion channel 1			
Aph-1a complex	Aph-1a	18 kDa microsomal signal peptidase subunit	Aph-1a	18 kDa microsomal signal peptidase subunit	Cerebral protein-10
		25 kDa microsomal signal peptidase subunit	APP	25 kDa microsomal signal peptidase subunit	CGI-13
		Aph-1a	Nicastrin	Brain-specific GTP-binding protein	KIAA0062
		APP	Pen-2	Cerebral protein-10	KIAA0251

		Brain-specific GTP-binding protein	Presenilin 1	CGI-13	KIAA0363
		Cerebral protein-10	Presenilin 2	Dihydrofolate reductase	KIAA0971
		CGI-13		Endocytic receptor Endo180	KIAA1250
		Dihydrofolate reductase		FLJ13660	Mesenchymal stem cell protein DSCD75
		Endocytic receptor Endo180		HU-K4	Protocadherin 7
		FLJ13660		Integral membrane protein 2B (ITM2B)	Protocadherin beta 16
		HU-K4		KIAA0062	Protocadherin beta 8
		Integral membrane protein 2B (ITM2B)		KIAA0251	Retinal short-chain dehydrogenase/reductase retSDR2
		KIAA0062		KIAA0363	Sterile alpha and repeat/armadillo motif protein

	KIAA0251		KIAA0971	Thioredoxin domain-containing protein
	KIAA0363		KIAA1250	Vacuolar ATP synthase membrane sector associated protein m8-9
	KIAA0971		Mesenchymal stem cell protein DSCD75	
	KIAA1250		Neurotropsin	
	Mesenchymal stem cell protein DSCD75		PP2C gamma	
	Neurotropsin		Protocadherin 7	
	Nicastrin		Protocadherin beta 16	
	Pen-2		Protocadherin beta 8	
	PP2C gamma		RAB-18	
	Presenilin 1		Rab3 GTPase-activating protein, non-catalytic subunit	

		Presenilin 2		Retinal short-chain dehydrogenase/reductase retSDR2	
		Protocadherin 7		Sideroflexin 1	
		Protocadherin beta 16		Signal transducer and activator of transcription-1	
		Protocadherin beta 8		SMAP-1B	
		RAB-18		Sterile alpha and heat/armadillo motif protein	
		Rab3 GTPase-activating protein, non-catalytic subunit		Sterol O-acyltransferase 1	
		Retinal short-chain dehydrogenase/reductase retSDR2		Thioredoxin domain-containing protein	
		Sideroflexin 1		Triple functional domain protein (PTPRF interacting)	

		Signal transducer and activator of transcription-1		Vacuolar ATP synthase membrane sector associated protein m8-9	
		SMAP-1B			
		Sterile alpha and heat/armadillo motif protein			
		Sterol O-acyltransferase 1			
		Thioredoxin domain-containing protein			
		Triple functional domain protein (PTPRF interacting)			
		Vacuolar ATP synthase membrane sector associated protein m8-9			
Aph-1b complex	Aph-1b	18 kDa microsomal signal peptidase subunit	Aph-1b	18 kDa microsomal signal peptidase subunit	Autocrine motility factor receptor

		23 kDa microsomal signal peptidase subunit	Nicastrin	23 kDa microsomal signal peptidase subunit	FLJ10737
		25 kDa microsomal signal peptidase subunit	Pen-2	25 kDa microsomal signal peptidase subunit	FLJ14560
		Activating transcription factor 6	Presenilin 1	Activating transcription factor 6	KIAA0363
		Aph-1a	Presenilin 2	Aph-1a	Protocadherin beta 8a
		Aph-1b		APP	Protocadherin gamma C3
		APP		Autocrine motility factor receptor	
		Autocrine motility factor receptor		Calsyntenin 1	
		Calsyntenin 1		cAMP responsive element binding protein-like 1	
		cAMP responsive element binding protein-like 1		Delta-1 catenin	

		Delta-1 catenin		FLJ10737	
		FLJ10737		FLJ14560	
		FLJ14560		HU-K4	
		HU-K4		KIAA0363	
		KIAA0363		PAS domain containing serine/threonine kinase	
		Nicastrin		Polycystin 2	
		PAS domain containing serine/threonine kinase		PP2C gamma	
		Pen-2		Protocadherin beta 8a	
		Polycystin 2		Protocadherin gamma C3	
		PP2C gamma		Voltage-dependent anion channel 3	
		Presenilin 1			
		Presenilin 2			
		Protocadherin beta 8a			
		Protocadherin gamma C3			

		Voltage-dependent anion channel 3				
Pen-2 complex	Pen-2	Alpha-2 catenin	Aph-1a	Alpha-2 catenin	KIAA1102	
		Aph-1a	Nicastrin	Copine III	MGC2803	
		Copine III	Pen-2	Dachshund 2	TNRC15	
		Dachshund 2	Presenilin 1	Delta-1 catenin		
		Delta-1 catenin		KIAA1102		
		KIAA1102		MGC2803		
		MGC2803		Presenilin 2		
		Nicastrin		TNRC15		
		Pen-2		TPST1		
		Presenilin 1		ZIP kinase		
		Presenilin 2				
		TNRC15				
		TPST1				
		ZIP kinase				
BACE1 D215N complex	BACE1 D215N	Acetylcholine receptor beta-4	BACE1 D215N	Acetylcholine receptor beta-4	MGC4248	
		ADP-ribosylation factor 4	Nicastrin	ADP-ribosylation factor 4	Protocadherin beta 7	

	APP		APP	
	BACE1 D215N		Calcium binding protein Cab45	
	Calcium binding protein Cab45		Delta-like homologue	
	Delta-like homologue		DNAJC3	
	DNAJC3		Fe65	
	Fe65		KIAA0747	
	KIAA0747		MGC4248	
	MGC4248		Neural cell adhesion molecule L1	
	Neural cell adhesion molecule L1		Neurotrophin	
	Neurotrophin		Protein amplified in osteosarcoma (OS-9)	
	Nicestrin		Protocadherin beta 10	
	Protein amplified in osteosarcoma (OS-9)		Protocadherin beta 14	
	Protocadherin beta 10		Protocadherin beta 7	
	Protocadherin beta 14		Protocadherin gamma C3	
	Protocadherin beta 7		S-100 alpha	

		Protocadherin gamma C3		Seipin	
		S-100 alpha		SEL-1 homologue	
		Seipin		Stromal cell-derived factor 2-like 1	
		SEL-1 homologue			
		Stromal cell-derived factor 2-like 1			
APP complex	APP	APP	APP	Bcl-XL-binding protein v68	FLJ10773
		Bcl-XL-binding protein v68	Fe65	FLJ10773	
		Fe65	Fe65L1	Neurotrypsin	
		Fe65L1	JIP-1	S-100 alpha	
		FLJ10773	X11beta	S-100 beta	
		JIP-1			
		Neurotrypsin			
		S-100 alpha			
		S-100 beta			
		X11beta			
APP695SW complex	APP695SW	APP695SW	APP695SW	FLJ10773	FLJ10773

		Fe65	Fe65	Integral membrane protein 2B (ITM2B)	
		Fe65L1	Fe65L1	S-100 alpha	
		FLJ10773	JIP-1		
		Integral membrane protein 2B (ITM2B)	X11beta		
		JIP-1			
		S-100 alpha			
		X11beta			
APP-C99 complex	APP-C99	APP	APP-C99		KIAA1102
		APP-C99	Fe65		KIAA1949
		Delta-like homologue	Fe65L1		MGC4022
		Fe65	X11beta		MGC5442
		Fe65L1			
		Integral membrane transporter protein			
		KIAA1102			
		KIAA1949			
		MGC4022			
		MGC5442			
		NAP-1 related protein			

		Neurocalcin delta				
		REST corepressor				
		S-100 alpha				
		S-100 beta				
		X11beta				
Tau complex	Tau	14-3-3 protein zeta/delta	14-3-3 protein zeta/delta	Deoxyhypusine synthase	MEP50	
		Actin	Actin	Dynactin 2		
		Alpha tubulin	Alpha tubulin	MEP50		
		Beta tubulin	Beta tubulin	Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1		
		Deoxyhypusine synthase	PPP2CA (PP2A, catalytic subunit, alpha)	PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)		
		Dynactin 2	PPP2CB (PP2A, catalytic subunit, beta)	S100 beta		
		MEP50	PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)			

		Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1	PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)		
		PPP2CA (PP2A, catalytic subunit, alpha)	Tau		
		PPP2CB (PP2A, catalytic subunit, beta)			
		PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)			
		PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)			
		S100 beta			
		Tau			
X11beta complex	X11beta	ADAMTS-19	APP	APLP1	ADAMTS-19
		APLP1	Munc18-1	ADAMTS-19	Cadherin EGF LAG seven-pass G-type receptor 2

	APP	Neurexin-1	Axonemal dynein heavy chain 8	Calsyntenin-2
	Axonemal dynein heavy chain 8	Syntaxin-1	Cadherin EGF LAG seven-pass G-type receptor 2	Calsyntenin-3
	Cadherin EGF LAG seven-pass G-type receptor 2	X11beta	Calsyntenin-1	ENG00000168820 (hypothetical protein with p-loop)
	Calsyntenin-1		Calsyntenin-2	FLJ13910
	Calsyntenin-2		Calsyntenin-3	HERC2 protein
	Calsyntenin-3		Chondroitin sulfate proteoglycan 6	HSPC154
	Chondroitin sulfate proteoglycan 6		Chromatin-specific transcription elongation factor FACT 140 kDa subunit	HSPC245
	Chromatin-specific transcription elongation factor FACT 140 kDa subunit		DC6 protein	KIAA0056
	DC6 protein		Dynein light chain-A	KIAA0166
	Dynein light chain 2A		Dynein light chain 2A	KIAA0564

		Dynein light chain-A		ENG00000168820 (hypothetical protein with p-loop)	KIAA0763
		ENG00000168820 (hypothetical protein with p-loop)		Eukaryotic translation initiation factor 4A, isoform	MEGF7
		Eukaryotic translation initiation factor 4A, isoform		FLJ13910	NIPSNAP1
		FLJ13910		FRAP1	Paladin
		FRAP1		GTP-binding protein ERA	PDZ and LIM domain protein 1
		GTP-binding protein ERA		HDAC2	PILT
		HDAC2		HERC2 protein	Programmed cell death 10
		HERC2 protein		HSPC154	Protein similar to AGCP6688
		HSPC154		HSPC245	Ubiquitin-protein ligase E3-alpha
		HSPC245		IKAP	

	IKAP		Insulinoma- glucagonoma protein 20	
	Insulinoma- glucagonoma protein 20		KIAA0056	
	KIAA0056		KIAA0166	
	KIAA0166		KIAA0325	
	KIAA0325		KIAA0564	
	KIAA0564		KIAA0763	
	KIAA0763		Laminin, gamma 1	
	Laminin, gamma 1		LIB (leucine-rich repeat protein)	
	LIB (leucine-rich repeat protein)		MBIP	
	MBIP		MEGF7	
	MEGF7		Myosin IXB	
	Munc18-1		NIPSNAP1	
	Myosin IXB		NIPSNAP2	
	Neurexin-1		Paladin	
	NIPSNAP1		PDZ and LIM domain protein 1	

		NIPSNAP2		Peroxiredoxin 4	
		Paladin		Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	
		PDZ and LIM domain protein 1		PILT	
		Peroxiredoxin 4		Procollagen C-endopeptidase enhancer	
		Phosphoenolpyruvate carboxykinase 2 (mitochondrial)		Programmed cell death 10	
		PILT		Protein similar to AGCP6688	
		Procollagen C-endopeptidase enhancer		Reelin	
		Programmed cell death 10		RPGR-interacting protein 1	
		Protein similar to AGCP6688		Serine/threonine protein phosphatase 6	

		Reelin			Sortilin-related receptor	
		RPGR-interacting protein 1			Synaptogyrin 3	
		Serine/threonine protein phosphatase 6			Ubiquitin-protein ligase E3-alpha	
		Sortilin-related receptor			VGF nerve growth factor inducible protein	
		Synaptogyrin 3			Zinc finger protein 198	
		Syntaxin-1				
		Ubiquitin-protein ligase E3-alpha				
		VGF nerve growth factor inducible protein				
		X11beta				
		Zinc finger protein 198				
Fe65 complex	Fe65	14-3-3 protein epsilon	APLP1		14-3-3 protein epsilon	Krab box protein ensp00000302970
		14-3-3 protein beta/alpha	APLP2		14-3-3 protein beta/alpha	Protein similar to probable mitotic centromere associated kinesin

		14-3-3 protein eta	APP		14-3-3 protein eta	Zinc finger protein 277
		14-3-3 protein gamma	APP-C99		14-3-3 protein gamma	
		14-3-3 protein tau	Fe65		14-3-3 protein tau	
		14-3-3 protein zeta/delta	RNB6		14-3-3 protein zeta/delta	
		APLP1	Transcription factor CP2		ATP-binding cassette, sub-family B, member 7	
		APLP2			ECP-51	
		APP			GAP-associated tyrosine phosphoprotein p62	
		APP-C99			Integral membrane protein 2B (ITM2B)	
		ATP-binding cassette, sub-family B, member 7			Krab box protein ensp00000302970	
		ECP-51			PDZ domain protein MAGI-3	

		Fe65		PPP2RBA (55 kDa regulatory subunit B, alpha)		
		GAP-associated tyrosine phosphoprotein p62		Protein similar to probable mitotic centromere associated kinesin		
		Integral membrane protein 2B (ITM2B)		Spliceosome protein SAP-62		
		Krab box protein ensp000000302970		Zinc finger protein 277		
		PDZ domain protein MAGI-3				
		PPP2RBA (55 kDa regulatory subunit B, alpha)				
		Protein similar to probable mitotic centromere associated kinesin				
		RNB6				

		Spliceosome protein SAP-62				
		Transcription factor CP2				
		Zinc finger protein 277				
Calsenilin complex	Calsenilin	C21ORF57	Calsenilin	C21ORF57	C21ORF57	
		Calsenilin	Presenilin 1	KCNQ2		
		KCNQ2		UDP- GalNAc:polypeptide N- acetylglactosaminyltr ansferase 7		
		Presenilin 1				
		UDP- GalNAc:polypeptide N- acetylglactosaminyltra nsferase 7				

TABLE 2

INDIVIDUAL PROTEINS OF THE COMPLEXES

Protein name	SEQ ID	IPI number	Molecular weight
14-3-3 protein epsilon	21	IP100000816.1	29174
14-3-3 protein beta/alpha	22	IP100013889.1	27951
14-3-3 protein eta	23	IP100030286.1	28088
14-3-3 protein gamma	24	IP100033598.1	28171
14-3-3 protein tau	25	IP100018146.1	27764
14-3-3 protein zeta/delta	26	IP100021263.1	27745
18 kDa microsomal signal peptidase subunit	98	IP100104128.1	20625
200 kDa proteasome activator	99	IP100005260.1	206407
23 kDa microsomal signal peptidase subunit	206	IP100030262.2	20253
25 kDa microsomal signal peptidase subunit	159	IP100014148.1	25003
Acetolactate synthase	103	IP1000009963.2	67868
Acetylcholine receptor beta-4	252	IP100097981.1	63202
Actin	240	IP100021439.1	41737
Activating transcription factor 6	207	IP100002511.1	74567
ADAMTS-19	44	IP100152639.1	134062
ADP-ribosylation factor 3	100	IP100029248.1	20470
ADP-ribosylation factor 4	251	IP100029743.1	20380

Adrenoleukodystrophy protein	104	IP100017637.1	82909
Alpha catenin	1	IP100017291.1	100071
Alpha tubulin	241	IP100142632.1	50152
Alpha-2 catenin	218	IP100030907.1	105282
Aph-1a	2	IP100059964.1	28996
Aph-1b	208	IP100103233.1	28460
APLP1	27	IP100020012.1	72202
APLP2	28	IP100031030.1	86956
APP	29	IP100006608.1	86943
APP695SW	232		78630
APP-C99	30		11277
ATP-binding cassette protein, sub-family B, member 1	101	IP100027481.1	141463
ATP-binding cassette, sub-family A, member 3	160	IP100017800.1	191388
ATP-binding cassette, sub-family B, member 7	31	IP100023879.1	82641
ATP-dependent metalloprotease FtsH1 homologue	102	IP100045946.1	86503
Autocrine motility factor receptor	209	IP100038908.1	73022
Axonemal dynein heavy chain 8	45	IP100014845.4	515950
BACE1	161	IP100011518.1	55764
BACE1 D215N	266		55764
BAX inhibitor 1	3	IP100022748.2	26538
Bcl-XL-binding protein v68	226	IP100063242.1	28006
Beta catenin	4	IP100017292.1	85497

Beta tubulin	242	IP100142634.1	49671
Brain-specific GTP-binding protein	187	IP100103530.1	63543
BSCv protein	162	IP100031131.1	46480
C21ORF57	262	IP100067923.1	33515
Cadherin EGF LAG seven-pass G-type receptor 2	46	IP100015346.1	317453
Cadherin-11 precursor	6	IP100024037.1	88049
Cadherin-4 precursor	7	IP100040836.3	74308
Calcium binding protein Cab45	253	IP100106646.1	41807
Calcium-binding protein P22	106	IP100016987.1	22325
Calsenilin	263	IP100032530.1	29231
Calsyntenin 1	47	IP100007257.1	109793
Calsyntenin-2	48	IP100005491.1	107020
Calsyntenin-3	49	IP100156997.1	106098
cAMP responsive element binding protein-like 1	217	IP100004084.3	76709
Casein kinase II beta chain	164	IP100010865.1	24942
Cathepsin B	165	IP100013478.1	37808
Cation-chloride cotransporter-interacting protein	107	IP100024998.1	96171
Centromere/kinetochore protein ZW10 homologue	108	IP100011631.1	88829
Cerebral protein-10	109	IP100018730.1	52118
CGI-13	163	IP100008847.1	52917
CGI-147	5	IP100032903.1	19194
CGI-51	105	IP100000985.1	51962

Chondroitin sulfate proteoglycan 6	50	IP100023102.1	141542
Chromatin-specific transcription elongation factor FACT 140 kDa subunit	51	IP100026970.1	119914
Copine III	219	IP100024403.1	60131
Dachshund 2	220	IP100065787.1	65323
DC6 protein	52	IP100024620.1	11529
Delta-1 catenin	8	IP100015202.1	104958
Delta-2 catenin	9	IP100033469.2	132665
Delta-6 fatty acid desaturase	166	IP100003544.1	52259
Delta-like homologue	233	IP100009191.1	41143
Deoxyhypusine synthase	243	IP100026829.1	40971
Dihydrofolate reductase	188	IP100016816.1	21322
DKFZp586c1924	110	IP100031064.1	21527
DNAJC3	254	IP100006713.1	57580
DOCK3	111	IP100004422.1	218952
Down syndrome critical region protein 2	112	IP100030770.1	32854
Dynactin 2	244	IP100013802.2	44231
Dynein light chain 2A	53	IP100023551.1	10922
Dynein light chain-A	54	IP100007675.1	56627
ECP-51	32	IP100009104.1	51157
ECSIT	113	IP100106506.1	49148
Endocytic receptor Endo180	189	IP100005707.3	166655
ENG00000168820 (hypothetical protein with p-loop)	55	IP100151716.2	30772

ENSG00000144840	167	IP100102897.1	26308
Eukaryotic translation initiation factor 4A, isoform	56	IP100025491.1	46154
Fe65	33	IP100010843.1	77244
Fe65L1	228	IP100023841.1	81080
FKRP	10	IP100013281.1	54568
FLJ10737	210	IP100018910.1	63336
FLJ10773	227	IP100018944.1	20345
FLJ13660	190	IP100100927.1	56921
FLJ13910	57	IP100009707.1	43993
FLJ13977	168	IP100025520.1	53482
FLJ14560	211	IP100013638.1	44876
FLJ20342	114	IP100015713.1	65084
FLJ20420	115	IP100015833.1	26152
FLJ20481	169	IP100016418.1	47655
FLJ20627	11	IP100016673.1	51618
FLJ22390	170	IP100009343.1	17098
FLJ22555	116	IP100103303.1	32545
FLJ22678	117	IP100002193.1	58355
FRAP1	58	IP100031410.1	288892
Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3	118	IP100014931.1	37062
Gamma catenin	12	IP100028128.1	81498
GAP-associated tyrosine phosphoprotein p62	34	IP100008575.1	48227

GTP-binding protein ERA	59	IP100026512.1	49098
HDAC2	60	IP100023289.1	55325
HERC2 protein	61	IP100005826.1	527472
HSPC154	62	IP100107156.1	28202
HSPC245	63	IP100025598.2	14124
HTRA2	119	IP100001663.1	48841
HU-K4	120	IP100163951.1	48771
Hypothetical protein tyrosine phosphatase ensg00000149185	171	IP100102935.1	22844
ICAM-2	172	IP100009477.1	30653
IKAP	64	IP100028877.1	150191
Insulinoma-glucagonoma protein 20	65	IP100103536.1	183267
Integral membrane protein 2B (ITM2B)	35	IP100031821.1	30338
Integral membrane transporter protein	234	IP100020093.1	31735
JIP-1	229	IP100023133.1	77524
KCNQ2	264	IP100012858.1	95848
KIAA0056	66	IP100000899.1	169718
KIAA0062	121	IP100014236.1	58417
KIAA0090	122	IP100160376.1	111759
KIAA0103	123	IP100014149.1	34833
KIAA0166	67	IP100001458.1	250749
KIAA0251	191	IP100010861.1	90027
KIAA0325	68	IP100141330.2	532367

KIAA0363		192	IP100004538.1	156999
KIAA0564		69	IP100158296.1	171891
KIAA0747		255	IP100022143.1	122856
KIAA0763		70	IP100006669.1	94914
KIAA0971		193	IP100007231.1	74536
KIAA1102		221	IP100160387.1	121739
KIAA1181		173	IP100003635.1	36879
KIAA1250		194	IP100033429.1	197211
KIAA1499		124	IP100001676.1	73788
KIAA1533		174	IP100001841.1	72964
KIAA1949		235	IP100150950.1	67959
Krab box protein ensp00000302970		36	IP100154267.1	37912
Laminin, gamma 1		72	IP100003398.1	177607
LIB (leucine-rich repeat protein)		71	IP100057018.2	64414
MBIP		73	IP100009868.1	39236
MEGF7		74	IP100023954.2	175609
MEP50		245	IP100012202.1	36724
Mesenchymal stem cell protein DSCD75		175	IP100010292.1	23865
MGC2803		222	IP100031526.1	18419
MGC4022		236	IP100010625.1	59797
MGC4248		125	IP100031582.1	24274
MGC5442		13	IP100027773.1	26261

Munc18-1	75	IP100046057.1	68736
Myosin IXB	76	IP100003064.1	228624
NAP-1 related protein	237	IP100155244.1	44159
Neural cell adhesion molecule L1	256	IP100027087.1	140003
Neurexin-1	79	IP100006314.1	161883
Neurocalcin delta	238	IP100149712.1	22114
Neurotrypsin	176	IP100011063.1	97012
Nicestrin	14	IP100021983.1	78411
NICE-3	126	IP100032413.1	28779
NIPSNAP1	77	IP100021086.2	33310
NIPSNAP2	78	IP100016077.1	33743
NPD002	127	IP100152981.1	68760
Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1	246	IP100002922.2	55595
P63 protein	128	IP100141318.1	66022
Paladin	82	IP100161782.1	96754
PAS domain containing serine/threonine kinase	212	IP100141040.1	142859
PDZ and LIM domain protein 1	80	IP100010414.2	36072
PDZ domain protein MAGI-3	37	IP100022491.1	111914
Pen-2	15	IP100020516.1	12029
Peroxiorexin 4	83	IP100011937.1	30540
Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	84	IP100004383.1	70637
PILT	81	IP100010544.2	60705

Plakophilin 4	16	IP100021076.1	134269
Polycystin 2	213	IP100013807.1	109790
PP1, regulatory subunit 15B	177	IP100045837.1	79125
PP2C gamma	195	IP100006167.1	59272
PPP2CA (PP2A, catalytic subunit, alpha)	247	IP100008380.1	35594
PPP2CB (PP2A, catalytic subunit, beta)	248	IP100003461.1	35575
PPP2R1A (PP2A, 65 kDa regulatory subunit A, alpha)	249	IP100025326.1	65092
PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)	38	IP100020852.1	51692
Presenilin 1	17	IP100026333.1	52163
Presenilin 2	152	IP100028485.1	50140
Procollagen C-endopeptidase enhancer	85	IP100014828.1	47972
Programmed cell death 10	86	IP100026997.1	24658
Prohibitin	153	IP100017334.1	29804
Protein amplified in osteosarcoma (OS-9)	178	IP100013268.1	75562
Protein similar to AGCP6688	87	IP100140709.1	14290
Protein similar to cholinergic receptor, nicotinic, alpha polypeptide 3	154	IP100007259.1	55637
Protein similar to probable mitotic centromere associated kinesin	39	IP100088667.1	126801
Protein similar to stromal cell-derived factor 2	179	IP100034198.1	23026
Protocadherin 7	196	IP100001893.2	116105
Protocadherin beta 10	257	IP100009034.1	87621
Protocadherin beta 14	258	IP100001434.1	87548
Protocadherin beta 16	197	IP100016595.1	84936

Protocadherin beta 7	259	IP100001425.1	86707
Protocadherin beta 8	180	IP100009033.1	87624
Protocadherin beta 8a	214	IP100045607.1	84983
Protocadherin gamma C3	215	IP100001872.3	101077
PSMA1	129	IP100016832.1	29556
PSMA3	130	IP100016834.1	28302
PSMA4	131	IP100016836.1	29484
PSMA6	132	IP100029623.1	27399
PSMB1	133	IP100025019.1	26489
PSMB2	134	IP100028006.1	22836
PSMB3	135	IP100028004.2	22949
PSMB4	136	IP100000806.1	29192
PSMB5	137	IP100000814.1	22897
PSMB6	138	IP100000811.2	25358
PSMC1	139	IP100011126.2	49185
PSMC2	140	IP100021435.1	48634
PSMC3	141	IP100018398.2	49204
PSMC4	142	IP100020042.2	47366
PSMC5	143	IP100023919.2	45626
PSMC6	144	IP100021926.2	44173
PSMD1	145	IP100015333.1	105866
PSMD11	146	IP100105598.1	47464

PSMD12	147	IP100003569.1	52904
PSMD13	148	IP100003570.1	42945
PSMD2	149	IP100012268.1	100200
PSMD3	150	IP100011603.2	60978
PSMD4	151	IP100022694.1	40737
RAB-18	198	IP100014577.1	22977
Rab3 GTPase-activating protein, non-catalytic subunit	199	IP100018280.3	155985
Reelin	89	IP100021018.1	388402
REP8 protein	181	IP100010353.1	30541
REST corepressor	239	IP100008531.1	53028
Retinal short-chain dehydrogenase/reductase retSDR2	183	IP100008260.1	32964
RING finger protein 5	182	IP100012608.1	19881
RNB6	40	IP100008862.1	44792
RPGR-interacting protein 1	88	IP100044777.1	103123
S-100 alpha	230	IP100010824.1	10415
S-100 beta	231	IP100023009.1	10582
SAP-62	41	IP100017341.2	49256
Seipin	261	IP100074114.1	51287
SEL-1 homologue	260	IP100002790.1	88755
Serine/threonine protein phosphatase 6	90	IP100012970.1	35144
Sideroflexin 1	201	IP100009368.2	35619
Signal transducer and activator of transcription-1	202	IP100030781.1	87335

SMAP-1B	200	IP100072534.1	103077
Sortilin 1	18	IP100016022.1	92100
Sortilin-related receptor	91	IP100022608.1	248441
Stearoyl-CoA desaturase	155	IP100100476.1	41523
Sterile alpha and HEAT/Armadillo motif protein	19	IP100007919.1	75337
Sterol O-acyltransferase 1	203	IP100019898.1	64763
Stromal cell-derived factor 2-like 1	184	IP100106642.2	23511
Synaptogyrin 3	92	IP100013947.1	24555
Syntaxin-1	93	IP100003370.1	33023
Tau	250	IP100025499.1	45850
Thioredoxin domain-containing protein	185	IP100001028.1	32535
TNRC15	223	IP100160501.1	127290
TPST1	224	IP100030106.1	42188
Transcription factor CP2	42	IP100037599.1	57256
Triple functional domain protein (PTPRF interacting)	204	IP100026676.1	324106
Ubiquilin	20	IP100099550.1	62519
Ubiquitin-protein ligase E3-alpha	94	IP100156938.1	83595
Ubiquitin-protein ligase EDD	156	IP100026320.1	309352
UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 7	265	IP100010104.1	75402
Vacuolar ATP synthase membrane sector associated protein m8-9	205	IP100041030.1	39036
VGF nerve growth factor inducible protein	95	IP100019628.1	67287
Voltage-dependent anion channel 1	186	IP100010430.1	30641

Voltage-dependent anion channel 2	157	IP100019625.1	31595
Voltage-dependent anion channel 3	216	IP100031804.1	30659
Wolframin	158	IP100008711.1	100306
X11beta	96	IP100017817.1	82512
Zinc finger protein 198	97	IP100032608.2	154911
Zinc finger protein 277	43	IP100016686.1	51615
ZIP kinase	225	IP100015213.1	52536

TABLE 3
BIOCHEMICAL ACTIVITIES OF THE COMPLEXES OF THE INVENTION

Name of complex	Biochemical Activity
Presenilin 1 complex	Gamma-secretase activity
Presenilin 2 complex	Gamma-secretase activity
Nicastrin complex	Gamma-secretase activity and assembly (trafficking)
Aph-1a complex	Gamma-secretase activity and assembly (trafficking)
Aph-1b complex	Gamma-secretase activity and assembly (trafficking)
Pen-2 complex	Gamma-secretase activity and assembly (trafficking)
BACE1 D215N complex	Beta-secretase activity
APP complex	Signalling activity (regulator of transcription)
APP695SW complex	Signalling activity (regulator of transcription)
APP-C99 complex	Signalling activity (regulator of transcription)
Tau complex	Regulator of microtubules and vesicle transport along microtubules
X11beta complex	Regulator of APP processing and APP function
Fe65 complex	Regulator of APP processing and APP function
Calsenilin complex	Regulator of transcription

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

Various publications are cited herein, the disclosures of which are incorporated by reference in their entireties.

REFERENCES

1. Kovacs, D.M., et al., *Alzheimer-associated presenilins 1 and 2: neuronal expression in brain and localization to intracellular membranes in mammalian cells*. Nat Med, 1996. 2(2): p. 224-9.
2. De Strooper, B., et al., *Deficiency of presenilin-1 inhibits the normal cleavage of amyloid precursor protein*. Nature, 1998. 391(6665): p. 387-90.
3. De Strooper, B., et al., *A presenilin-1-dependent gamma-secretase-like protease mediates release of Notch intracellular domain*. Nature, 1999. 398(6727): p. 518-22.
4. Ray, W.J., et al., *Evidence for a physical interaction between presenilin and notch*. Proc Natl Acad Sci USA, 1999. 96(6): p. 3263-8.
5. Georgakopoulos, A., et al., *Presenilin-1 forms complexes with the cadherin/catenin cell-cell adhesion system and is recruited to intercellular and synaptic contacts*. Mol Cell, 1999. 4(6): p. 893-902.
6. Zhang, Z., et al., *Destabilization of beta-catenin by mutations in presenilin-1 potentiates neuronal apoptosis*. Nature, 1998. 395(6703): p. 698-702.
7. Yu, G., et al., *The presenilin 1 protein is a component of a high molecular weight intracellular complex that contains beta-catenin*. J Biol Chem, 1998. 273(26): p. 16470-5.
8. Zhou, J., et al., *Presenilin 1 interaction in the brain with a novel member of the Armadillo family*. Neuroreport, 1997. 8(8): p. 2085-90.
9. Levesque, G., et al., *Presenilins interact with armadillo proteins including neural-specific plakophilin-related protein and beta-catenin*. J Neurochem, 1999. 72(3): p. 999-1008.
10. Tanahashi, H. and T. Tabira, *Isolation of human delta-catenin and its binding specificity with presenilin 1*. Neuroreport, 1999. 10(3): p. 563-8.
11. Xia, W., et al., *Interaction between amyloid precursor protein and presenilins in mammalian cells: implications for the pathogenesis of Alzheimer disease*. Proc Natl Acad Sci USA, 1997. 94(15): p. 8208-13.
12. Yu, G., et al., *Nicastrin modulates presenilin-mediated notch/glp-1 signal transduction and betaAPP processing*. Nature, 2000. 407(6800): p. 48-54.
13. Francis, R., et al., *aph-1 and pen-2 are required for Notch pathway signaling, gamma-secretase cleavage of betaAPP, and presenilin protein accumulation*. Dev Cell, 2002. 3(1): p. 85-97.
14. Goutte, C., et al., *APH-1 is a multipass membrane protein essential for the Notch signaling pathway in Caenorhabditis elegans embryos*. Proc Natl Acad Sci U S A, 2002. 99(2): p. 775-9.
15. Kopan, R. and A. Goate, *A common enzyme connects notch signaling and Alzheimer's disease*. Genes Dev, 2000. 14(22): p. 2799-806.

16. Esler, W.P., et al., *Activity-dependent isolation of the presenilin- gamma -secretase complex reveals nicastrin and a gamma substrate*. Proc Natl Acad Sci U S A, 2002. **99**(5): p. 2720-5.
17. Citron, M., et al., *Mutant presenilins of Alzheimer's disease increase production of 42-residue amyloid beta-protein in both transfected cells and transgenic mice*. Nat Med, 1997. **3**(1): p. 67-72.
18. Jarrett, J.T., E.P. Berger, and P.T. Lansbury, Jr., *The carboxy terminus of the beta amyloid protein is critical for the seeding of amyloid formation: implications for the pathogenesis of Alzheimer's disease*. Biochemistry, 1993. **32**(18): p. 4693-7.
19. Satoh, J. and Y. Kuroda, *Nicastrin, a key regulator of presenilin function, is expressed constitutively in human neural cell lines*. Neuropathology, 2001. **21**(2): p. 115-22.
20. Chen, F., et al., *Nicastrin binds to membrane-tethered Notch*. Nat Cell Biol, 2001. **3**(8): p. 751-4.
21. Lopez-Schier, H. and D. St Johnston, *Drosophila nicastrin is essential for the intramembranous cleavage of notch*. Dev Cell, 2002. **2**(1): p. 79-89.
22. Chung, H.M. and G. Struhl, *Nicastrin is required for Presenilin-mediated transmembrane cleavage in Drosophila*. Nat Cell Biol, 2001. **3**(12): p. 1129-32.
23. Hu, Y., Y. Ye, and M.E. Fortini, *Nicastrin is required for gamma-secretase cleavage of the Drosophila Notch receptor*. Dev Cell, 2002. **2**(1): p. 69-78.
24. Lee, S.F., et al., *Mammalian APh-1 interacts with presenilin and nicastrin, and is required for intramembrane proteolysis of APP and Notch*. J Biol Chem, 2002. **277**: p. 23.
25. Leem, J.Y., et al., *Presenilin 1 is required for maturation and cell surface accumulation of nicastrin*. J Biol Chem, 2002. **277**: p. 19236-40.
26. Tomita, T., et al., *Complex N-glycosylated form of nicastrin is stabilized and selectively bound to presenilin fragments*. FEBS Lett, 2002. **520**(1-3): p. 117-21.
27. Edbauer, D., et al., *Presenilin and nicastrin regulate each other and determine amyloid beta-peptide production via complex formation*. Proc Natl Acad Sci U S A, 2002. **99**(13): p. 8666-71.
28. Yang, D.S., et al., *Mature glycosylation and trafficking of nicastrin modulate its binding to presenilins*. J Biol Chem, 2002. **277**(31): p. 28135-42.
29. Kimberly, W.T., et al., *Complex N-linked glycosylated Nicastrin associates with active gamma -secretase and undergoes tight cellular regulation*. J Biol Chem, 2002. **277**: p. 35113-7.
30. Steiner, H., et al., *PEN-2 is an integral component of the gamma -secretase complex required for coordinated expression of presenilin and nicastrin*. J Biol Chem, 2002: p. 39062-5.

31. Vassar, R., et al., *Beta-secretase cleavage of Alzheimer's amyloid precursor protein by the transmembrane aspartic protease BACE*. Science, 1999. **286**(5440): p. 735-41.
32. Roberds, S.L., et al., *BACE knockout mice are healthy despite lacking the primary beta-secretase activity in brain: implications for Alzheimer's disease therapeutics*. Hum Mol Genet, 2001. **10**(12): p. 1317-24.
33. Huse, J.T., et al., *Maturation and endosomal targeting of beta-site amyloid precursor protein-cleaving enzyme. The Alzheimer's disease beta-secretase*. J Biol Chem, 2000. **275**(43): p. 33729-37.
34. Bennett, B.D., et al., *A furin-like convertase mediates propeptide cleavage of BACE, the Alzheimer's beta -secretase*. J Biol Chem, 2000. **275**(48): p. 37712-7.
35. Masters, C.L., et al., *Amyloid plaque core protein in Alzheimer disease and Down syndrome*. Proc Natl Acad Sci U S A, 1985. **82**(12): p. 4245-9.
36. Van Nostrand, W.E., et al., *Protease nexin-II, a potent antichymotrypsin, shows identity to amyloid beta-protein precursor*. Nature, 1989. **341**(6242): p. 546-9.
37. Multhaup, G., et al., *The amyloid precursor protein of Alzheimer's disease in the reduction of copper(II) to copper(I)*. Science, 1996. **271**(5254): p. 1406-9.
38. Yan, S.D., et al., *RAGE and amyloid-beta peptide neurotoxicity in Alzheimer's disease*. Nature, 1996. **382**(6593): p. 685-91.
39. Kaneko, I., et al., *Suppression of mitochondrial succinate dehydrogenase, a primary target of beta-amyloid, and its derivative racemized at Ser residue*. J Neurochem, 1995. **65**(6): p. 2585-93.
40. Bertram, L. and R.E. Tanzi, *Dancing in the dark? The status of late-onset Alzheimer's disease genetics*. J Mol Neurosci, 2001. **17**(2): p. 127-36.
41. De Jonghe, C., et al., *Flemish and Dutch mutations in amyloid beta precursor protein have different effects on amyloid beta secretion*. Neurobiol Dis, 1998. **5**(4): p. 281-6.
42. Cao, X. and T.C. Sudhof, *A transcriptionally [correction of transcriptively] active complex of APP with Fe65 and histone acetyltransferase Tip60*. Science, 2001. **293**(5527): p. 115-20.
43. Baek, S.H., et al., *Exchange of N-CoR corepressor and Tip60 coactivator complexes links gene expression by NF-kappaB and beta-amyloid precursor protein*. Cell, 2002. **110**(1): p. 55-67.
44. Kinoshita, A., et al., *The gamma secretase-generated carboxyl-terminal domain of the amyloid precursor protein induces apoptosis via Tip60 in H4 cells*. J Biol Chem, 2002. **277**(32): p. 28530-6.
45. Weggen, S., et al., *A subset of NSAIDs lower amyloidogenic Abeta42 independently of cyclooxygenase activity*. Nature, 2001. **414**(6860): p. 212-6.

46. Buxbaum, J.D., et al., *Calsenilin: a calcium-binding protein that interacts with the presenilins and regulates the levels of a presenilin fragment*. Nat Med, 1998. 4(10): p. 1177-81.
47. An, W.F., et al., *Modulation of A-type potassium channels by a family of calcium sensors*. Nature, 2000. 403(6769): p. 553-6.
48. Cheng, H.Y., et al., *DREAM is a critical transcriptional repressor for pain modulation*. Cell, 2002. 108(1): p. 31-43.
49. Alonso, A.C., I. Grundke-Iqbal, and K. Iqbal, *Alzheimer's disease hyperphosphorylated tau sequesters normal tau into tangles of filaments and disassembles microtubules*. Nat Med, 1996. 2(7): p. 783-7.
50. McLoughlin, D.M. and C.C. Miller, *The intracellular cytoplasmic domain of the Alzheimer's disease amyloid precursor protein interacts with phosphotyrosine-binding domain proteins in the yeast two-hybrid system*. FEBS Lett, 1996. 397(2-3): p. 197-200.
51. Scheinfeld, M.H., et al., *Processing of beta -Amyloid Precursor Like Protein-1 and -2 by hgamma -secretase regulates transcription*. J Biol Chem, 2002.
52. Sabo, S.L., et al., *Regulation of beta-amyloid secretion by FE65, an amyloid protein precursor-binding protein*. J Biol Chem, 1999. 274(12): p. 7952-7.
53. Kimberly, W.T., et al., *The intracellular domain of the beta-amyloid precursor protein is stabilized by Fe65 and translocates to the nucleus in a notch-like manner*. J Biol Chem, 2001. 276(43): p. 40288-92.
54. Zambrano, N., et al., *The Fe65 adaptor protein interacts through its PID1 domain with the transcription factor CP2/LSF/LBP1*. J Biol Chem, 1998. 273(32): p. 20128-33.
55. Trommsdorff, M., et al., *Interaction of cytosolic adaptor proteins with neuronal apolipoprotein E receptors and the amyloid precursor protein*. J Biol Chem, 1998. 273(50): p. 33556-60.
56. Bruni, P., et al., *Fe65, a ligand of the Alzheimer's beta-amyloid precursor protein, blocks cell cycle progression by down-regulating thymidylate synthase expression*. J Biol Chem, 2002. 277(38): p. 35481-8.
57. Biederer, T. and T.C. Sudhof, *Mints as adaptors. Direct binding to neurexins and recruitment of munc18*. J Biol Chem, 2000. 275(51): p. 39803-6.
58. Ho, C.S., et al., *Synergistic effects of Munc18a and X11 proteins on amyloid precursor protein metabolism*. J Biol Chem, 2002. 277(30): p. 27021-8.
59. Sastre, M., R.S. Turner, and E. Levy, *X11 interaction with beta-amyloid precursor protein modulates its cellular stabilization and reduces amyloid beta-protein secretion*. J Biol Chem, 1998. 273(35): p. 22351-7.
60. Lee, D.S., et al., *Regulation of X11L-dependent amyloid precursor protein metabolism by XB51, a novel X11L-binding protein*. J Biol Chem, 2000. 275(30): p. 23134-8.

61. Hase, M., et al., *Expression and characterization of the Drosophila X11-like/Mint protein during neural development*. J Neurochem, 2002. **81**(6): p. 1223-32.
62. Tomita, S., et al., *PDZ domain-dependent suppression of NF-kappaB/p65-induced Abeta42 production by a neuron-specific X11-like protein*. J Biol Chem, 2000. **275**(17): p. 13056-60.

CLAIMS

1. A protein complex selected from complex (I) and comprising
 - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
 - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions;and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, second column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm

DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising the proteins selected from the proteins in table 1, third column or a homologue thereof, or a variant thereof or functionally active fragments or functionally active derivatives of said proteins, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, but 1 to the number of proteins listed in table 1, fifth column of said complex, or a homologue or a variant thereof, or a functionally active fragment or functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins of said fifth column under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

5. The complex of any of claims 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of claim 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of claims 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of claims 1 - 7 that is involved in the biochemical activity as stated in table 3.
9. A process for preparing a complex of any of claims 1 - 8 and optionally the components thereof comprising the following steps:
expressing a protein of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the protein, preferably a tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to claim 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of claims 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of claims 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a

functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to claim 13.
15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to claim 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to claim 1 (a) and at least one of said proteins, being selected from the second group of proteins according to claim 1 (b).
16. Host cell, containing a vector comprising at least one of the nucleic acid of claim 14 and /or a construct of claim 15 or containing several vectors each comprising at least the nucleic acid encoding at least one protein selected from the first group of proteins according to claim 1 (a) and the nucleic acid encoding at least one protein selected from the second group of proteins according to claim 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, which binds the complex of any of claims 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and/or an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the group of proteins according to claim 13.

18. A kit comprising in one or more containers the complex of any of claims 1 - 8 and/or the proteins of claim 13, optionally together with an antibody according to claim 17 and/or further components such as reagents and working instructions.
19. The kit according to claim 18 for processing a substrate of a complex of any one of claims 1 - 8.
20. The kit according to claim 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
21. Array in which at least a complex according to any of claims 1 - 8 and/or at least one protein according to claim 13 and/or at least one antibody according to claim 17 is attached to a solid carrier.
22. A process for processing a substrate of a complex of any one of claims 1 - 8 comprising the step of bringing into contact a complex to any of claims 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of claims 1 - 8 and/or any of the proteins according to claim 13.
24. A pharmaceutical composition according to claim 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
25. A method for screening for a molecule that binds to the complex of any one of claims 1 - 8 and/or any of the proteins of claim 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of claims 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of claim 26, wherein the amount of said complex is determined.
28. The method of claim 26, wherein the activity of said complex is determined.
29. The method of claim 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of claim 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of claim 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of claims 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of claims 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of claims 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the claims 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample

from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of claim 35, wherein the amount of said complex is determined.
37. The method of claim 35, wherein the activity of said complex is determined.
38. The method of claim 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of claim 35, wherein the amount of the individual protein components of said complex are determined.
40. The method of claim 39, wherein said determining step comprises determining whether any of the proteins according to claim 13 is present in the complex.
41. The complex of any one of claims 1 - 8, or proteins of claim 13 or the antibody of fragment of claim 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of claims 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity or, or protein components of, said complex.
43. The method according to claim 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to claim 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of claims 1 - 8 and/or any of the proteins listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease and related neurodegenerative disorders.

Protein Complexes associated with APP-processing
SEQUENCE LISTING

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<130> Protein Complexes associated with APP-processing

<160> 266

<170> PatentIn version 3.1

<210> 1

<211> 906

<212> PRT

<213> Homo sapiens

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Met Thr Ala Val His Ala Gly Asn Ile Asn Phe Lys Trp Asp Pro Lys
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Ser Leu Glu Ile Arg Thr Leu Ala Val Glu Arg Leu Leu Glu Pro Leu
20 25 30

Val Thr Gln Val Thr Thr Leu Val Asn Thr Asn Ser Lys Gly Pro Ser
35 40 45

Asn Lys Lys Arg Gly Arg Ser Lys Lys Ala His Val Leu Ala Ala Ser
50 55 60

Val Glu Gln Ala Thr Glu Asn Phe Leu Glu Lys Gly Asp Lys Ile Ala
65 70 75 80

Lys Glu Ser Gln Phe Leu Lys Glu Glu Leu Val Ala Ala Val Glu Asp
85 90 95

Val Arg Lys Gln Gly Asp Leu Met Lys Ala Ala Ala Gly Glu Phe Ala
100 105 110

Asp Asp Pro Cys Ser Ser Val Lys Arg Gly Asn Met Val Arg Ala Ala
115 120 125

Protein Complexes associated with APP-processing

Arg Ala Leu Leu Ser Ala Val Thr Arg Leu Leu Ile Leu Ala Asp Met
 130 135 140
 Ala Asp Val Tyr Lys Leu Leu Val Gln Leu Lys Val Val Glu Asp Gly
 145 150 155 160
 Ile Leu Lys Leu Arg Asn Ala Gly Asn Glu Gln Asp Leu Gly Ile Gln
 165 170 175
 Tyr Lys Ala Leu Lys Pro Glu Val Asp Lys Leu Asn Ile Met Ala Ala
 180 185 190
 Lys Arg Gln Gln Glu Leu Lys Asp Val Gly His Arg Asp Gln Met Ala
 195 200 205
 Ala Ala Arg Gly Ile Leu Gln Lys Asn Val Pro Ile Leu Tyr Thr Ala
 210 215 220
 Ser Gln Ala Cys Leu Gln His Pro Asp Val Ala Ala Tyr Lys Ala Asn
 225 230 235 240
 Arg Asp Leu Ile Tyr Lys Gln Leu Gln Gln Ala Val Thr Gly Ile Ser
 245 250 255
 Asn Ala Ala Gln Ala Thr Ala Ser Asp Asp Ala Ser Gln His Gln Gly
 260 265 270
 Gly Gly Gly Gly Glu Leu Ala Tyr Ala Leu Asn Asn Phe Asp Lys Gln
 275 280 285
 Ile Ile Val Asp Pro Leu Ser Phe Ser Glu Glu Arg Phe Arg Pro Ser
 290 295 300
 Leu Glu Glu Arg Leu Glu Ser Ile Ile Ser Gly Ala Ala Leu Met Ala
 305 310 315 320
 Asp Ser Ser Cys Thr Arg Asp Asp Arg Arg Glu Arg Ile Val Ala Glu
 325 330 335
 Cys Asn Ala Val Arg Gln Ala Leu Gln Asp Leu Leu Ser Glu Tyr Met
 340 345 350
 Gly Asn Ala Gly Arg Lys Glu Arg Ser Asp Ala Leu Asn Ser Ala Ile
 355 360 365
 Asp Lys Met Thr Lys Lys Thr Arg Asp Leu Arg Arg Gln Leu Arg Lys
 370 375 380
 Ala Val Met Asp His Val Ser Asp Ser Phe Leu Glu Thr Asn Val Pro
 385 390 395 400

Protein Complexes associated with APP-processing

Leu Leu Val Leu Ile Glu Ala Ala Lys Asn Gly Asn Glu Lys Glu Val
405 410 415

Lys Glu Tyr Ala Gln Val Phe Arg Glu His Ala Asn Lys Leu Ile Glu
420 425 430

Val Ala Asn Leu Ala Cys Ser Ile Ser Asn Asn Glu Glu Gly Val Lys
435 440 445

Leu Val Arg Met Ser Ala Ser Gln Leu Glu Ala Leu Cys Pro Gln Val
450 455 460

Ile Asn Ala Ala Leu Ala Leu Ala Ala Lys Pro Gln Ser Lys Leu Ala
465 470 475 480

Gln Glu Asn Met Asp Leu Phe Lys Glu Gln Trp Glu Lys Gln Val Arg
485 490 495

Val Leu Thr Asp Ala Val Asp Asp Ile Thr Ser Ile Asp Asp Phe Leu
500 505 510

Ala Val Ser Glu Asn His Ile Leu Glu Asp Val Asn Lys Cys Val Ile
515 520 525

Ala Leu Gln Glu Lys Asp Val Asp Gly Leu Asp Arg Thr Ala Gly Ala
530 535 540

Ile Arg Gly Arg Ala Ala Arg Val Ile His Val Val Thr Ser Glu Met
545 550 555 560

Asp Asn Tyr Glu Pro Gly Val Tyr Thr Glu Lys Val Leu Glu Ala Thr
565 570 575

Lys Leu Leu Ser Asn Thr Val Met Pro Arg Phe Thr Glu Gln Val Glu
580 585 590

Ala Ala Val Glu Ala Leu Ser Ser Asp Pro Ala Gln Pro Met Asp Glu
595 600 605

Asn Glu Phe Ile Asp Ala Ser Arg Leu Val Tyr Asp Gly Ile Arg Asp
610 615 620

Ile Arg Lys Ala Val Leu Met Ile Arg Thr Pro Glu Glu Leu Asp Asp
625 630 635 640

Ser Asp Phe Glu Thr Glu Asp Phe Asp Val Arg Ser Arg Thr Ser Val
645 650 655

Gln Thr Glu Asp Asp Gln Leu Ile Ala Gly Gln Ser Ala Arg Ala Ile
660 665 670

Protein Complexes associated with APP-processing
 Met Ala Gln Leu Pro Gln Glu Gln Lys Ala Lys Ile Ala Glu Gln Val
 675 680 685

Ala Ser Phe Gln Glu Glu Lys Ser Lys Leu Asp Ala Glu Val Ser Lys
 690 695 700

Trp Asp Asp Ser Gly Asn Asp Ile Ile Val Leu Ala Lys Gln Met Cys
 705 710 715 720

Met Ile Met Met Glu Met Thr Asp Phe Thr Arg Gly Lys Gly Pro Leu
 725 730 735

Lys Asn Thr Ser Asp Val Ile Ser Ala Ala Lys Lys Ile Ala Glu Ala
 740 745 750

Gly Ser Arg Met Asp Lys Leu Gly Arg Thr Ile Ala Asp His Cys Pro
 755 760 765

Asp Ser Ala Cys Lys Gln Asp Leu Leu Ala Tyr Leu Gln Arg Ile Ala
 770 775 780

Leu Tyr Cys His Gln Leu Asn Ile Cys Ser Lys Val Lys Ala Glu Val
 785 790 795 800

Gln Asn Leu Gly Gly Glu Leu Val Val Ser Gly Val Asp Ser Ala Met
 805 810 815

Ser Leu Ile Gln Ala Ala Lys Asn Leu Met Asn Ala Val Val Gln Thr
 820 825 830

Val Lys Ala Ser Tyr Val Ala Ser Thr Lys Tyr Gln Lys Ser Gln Gly
 835 840 845

Met Ala Ser Leu Asn Leu Pro Ala Val Ser Trp Lys Met Lys Ala Pro
 850 855 860

Glu Lys Lys Pro Leu Val Lys Arg Glu Lys Gln Asp Glu Thr Gln Thr
 865 870 875 880

Lys Ile Lys Arg Ala Ser Gln Lys Lys His Val Asn Pro Val Gln Ala
 885 890 895

Leu Ser Glu Phe Lys Ala Met Asp Ser Ile
 900 905

<210> 2

<211> 265

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

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 1 5 10 15

Ala Phe Ala Leu Phe Leu Ile Thr Val Ala Gly Asp Pro Leu Arg Val
 20 25 30

Ile Ile Leu Val Ala Gly Ala Phe Phe Trp Leu Val Ser Leu Leu Leu
 35 40 45

Ala Ser Val Val Trp Phe Ile Leu Val His Val Thr Asp Arg Ser Asp
 50 55 60

Ala Arg Leu Gln Tyr Gly Leu Leu Ile Phe Gly Ala Ala Val Ser Val
 65 70 75 80

Leu Leu Gln Glu Val Phe Arg Phe Ala Tyr Tyr Lys Leu Leu Lys Lys
 85 90 95

Ala Asp Glu Gly Leu Ala Ser Leu Ser Glu Asp Gly Arg Ser Pro Ile
 100 105 110

Ser Ile Arg Gln Met Ala Tyr Val Ser Gly Leu Ser Phe Gly Ile Ile
 115 120 125

Ser Gly Val Phe Ser Val Ile Asn Ile Leu Ala Asp Ala Leu Gly Pro
 130 135 140

Gly Val Val Gly Ile His Gly Asp Ser Pro Tyr Tyr Phe Leu Thr Ser
 145 150 155 160

Ala Phe Leu Thr Ala Ala Ile Ile Leu Leu His Thr Phe Trp Gly Val
 165 170 175

Val Phe Phe Asp Ala Cys Glu Arg Arg Arg Tyr Trp Ala Leu Gly Leu
 180 185 190

Val Val Gly Ser His Leu Leu Thr Ser Gly Leu Thr Phe Leu Asn Pro
 195 200 205

Trp Tyr Glu Ala Ser Leu Leu Pro Ile Tyr Ala Val Thr Val Ser Met
 210 215 220

Gly Leu Trp Ala Phe Ile Thr Ala Gly Gly Ser Leu Arg Ser Ile Gln
 225 230 235 240

Arg Ser Leu Leu Cys Arg Arg Gln Glu Asp Ser Arg Val Met Val Tyr
 245 250 255

Protein Complexes associated with APP-processing
 Ser Ala Leu Arg Ile Pro Pro Glu Asp
 260 265

<210> 3

<211> 237

<212> PRT

<213> Homo sapiens

<400> 3

Met Asn Ile Phe Asp Arg Lys Ile Asn Phe Asp Ala Leu Leu Lys Phe
 1 5 10 15

Ser His Ile Thr Pro Ser Thr Gln Gln His Leu Lys Lys Val Tyr Ala
 20 25 30

Ser Phe Ala Leu Cys Met Phe Val Ala Ala Ala Gly Ala Tyr Val His
 35 40 45

Met Val Thr His Phe Ile Gln Ala Gly Leu Leu Ser Ala Leu Gly Ser
 50 55 60

Leu Ile Leu Met Ile Trp Leu Met Ala Thr Pro His Ser His Glu Thr
 65 70 75 80

Glu Gln Lys Arg Leu Gly Leu Leu Ala Gly Phe Ala Phe Leu Thr Gly
 85 90 95

Val Gly Leu Gly Pro Ala Leu Glu Phe Cys Ile Ala Val Asn Pro Ser
 100 105 110

Ile Leu Pro Thr Ala Phe Met Gly Thr Ala Met Ile Phe Thr Cys Phe
 115 120 125

Thr Leu Ser Ala Leu Tyr Ala Arg Arg Arg Ser Tyr Leu Phe Leu Gly
 130 135 140

Gly Ile Leu Met Ser Ala Leu Ser Leu Leu Leu Ser Ser Leu Gly
 145 150 155 160

Asn Val Phe Phe Gly Ser Ile Trp Leu Phe Gln Ala Asn Leu Tyr Val
 165 170 175

Gly Leu Val Val Met Cys Gly Phe Val Leu Phe Asp Thr Gln Leu Ile
 180 185 190

Ile Glu Lys Ala Glu His Gly Asp Gln Asp Tyr Ile Trp His Cys Ile
 195 200 205

Protein Complexes associated with APP-processing
 Asp Leu Phe Leu Asp Phe Ile Thr Val Phe Arg Lys Leu Met Met Ile
 210 215 220

Leu Ala Met Asn Glu Lys Asp Lys Lys Lys Glu Lys Lys
 225 230 235

<210> 4

<211> 781

<212> PRT

<213> Homo sapiens

<400> 4

Met Ala Thr Gln Ala Asp Leu Met Glu Leu Asp Met Ala Met Glu Pro
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Asp Arg Lys Ala Ala Val Ser His Trp Gln Gln Gln Ser Tyr Leu Asp
 20 25 30

Ser Gly Ile His Ser Gly Ala Thr Thr Thr Ala Pro Ser Leu Ser Gly
 35 40 45

Lys Gly Asn Pro Glu Glu Glu Asp Val Asp Thr Ser Gln Val Leu Tyr
 50 55 60

Glu Trp Glu Gln Gly Phe Ser Gln Ser Phe Thr Gln Glu Gln Val Ala
 65 70 75 80

Asp Ile Asp Gly Gln Tyr Ala Met Thr Arg Ala Gln Arg Val Arg Ala
 85 90 95

Ala Met Phe Pro Glu Thr Leu Asp Glu Gly Met Gln Ile Pro Ser Thr
 100 105 110

Gln Phe Asp Ala Ala His Pro Thr Asn Val Gln Arg Leu Ala Glu Pro
 115 120 125

Ser Gln Met Leu Lys His Ala Val Val Asn Leu Ile Asn Tyr Gln Asp
 130 135 140

Asp Ala Glu Leu Ala Thr Arg Ala Ile Pro Glu Leu Thr Lys Leu Leu
 145 150 155 160

Asn Asp Glu Asp Gln Val Val Val Asn Lys Ala Ala Val Met Val His
 165 170 175

Gln Leu Ser Lys Lys Glu Ala Ser Arg His Ala Ile Met Arg Ser Pro
 180 185 190

Protein Complexes associated with APP-processing

Gln Met Val Ser Ala Ile Val Arg Thr Met Gln Asn Thr Asn Asp Val
 195 200 205

Glu Thr Ala Arg Cys Thr Ala Gly Thr Leu His Asn Leu Ser His His
 210 215 220

Arg Glu Gly Leu Leu Ala Ile Phe Lys Ser Gly Gly Ile Pro Ala Leu
 225 230 235 240

Val Lys Met Leu Gly Ser Pro Val Asp Ser Val Leu Phe Tyr Ala Ile
 245 250 255

Thr Thr Leu His Asn Leu Leu Leu His Gln Glu Gly Ala Lys Met Ala
 260 265 270

Val Arg Leu Ala Gly Gly Leu Gln Lys Met Val Ala Leu Leu Asn Lys
 275 280 285

Thr Asn Val Lys Phe Leu Ala Ile Thr Thr Asp Cys Leu Gln Ile Leu
 290 295 300

Ala Tyr Gly Asn Gln Glu Ser Lys Leu Ile Ile Leu Ala Ser Gly Gly
 305 310 315 320

Pro Gln Ala Leu Val Asn Ile Met Arg Thr Tyr Thr Tyr Glu Lys Leu
 325 330 335

Leu Trp Thr Thr Ser Arg Val Leu Lys Val Leu Ser Val Cys Ser Ser
 340 345 350

Asn Lys Pro Ala Ile Val Glu Ala Gly Gly Met Gln Ala Leu Gly Leu
 355 360 365

His Leu Thr Asp Pro Ser Gln Arg Leu Val Gln Asn Cys Leu Trp Thr
 370 375 380

Leu Arg Asn Leu Ser Asp Ala Ala Thr Lys Gln Glu Gly Met Glu Gly
 385 390 395 400

Leu Leu Gly Thr Leu Val Gln Leu Leu Gly Ser Asp Asp Ile Asn Val
 405 410 415

Val Thr Cys Ala Ala Gly Ile Leu Ser Asn Leu Thr Cys Asn Asn Tyr
 420 425 430

Lys Asn Lys Met Met Val Cys Gln Val Gly Gly Ile Glu Ala Leu Val
 435 440 445

Arg Thr Val Leu Arg Ala Gly Asp Arg Glu Asp Ile Thr Glu Pro Ala
 450 455 460

Protein Complexes associated with APP-processing

Ile Cys Ala Leu Arg His Leu Thr Ser Arg His Gln Glu Ala Glu Met
 465 470 475 480

Ala Gln Asn Ala Val Arg Leu His Tyr Gly Leu Pro Val Val Val Lys
 485 490 495

Leu Leu His Pro Pro Ser His Trp Pro Leu Ile Lys Ala Thr Val Gly
 500 505 510

Leu Ile Arg Asn Leu Ala Leu Cys Pro Ala Asn His Ala Pro Leu Arg
 515 520 525

Glu Gln Gly Ala Ile Pro Arg Leu Val Gln Leu Leu Val Arg Ala His
 530 535 540

Gln Asp Thr Gln Arg Arg Thr Ser Met Gly Gly Thr Gln Gln Gln Phe
 545 550 555 560

Val Glu Gly Val Arg Met Glu Glu Ile Val Glu Gly Cys Thr Gly Ala
 565 570 575

Leu His Ile Leu Ala Arg Asp Val His Asn Arg Ile Val Ile Arg Gly
 580 585 590

Leu Asn Thr Ile Pro Leu Phe Val Gln Leu Leu Tyr Ser Pro Ile Glu
 595 600 605

Asn Ile Gln Arg Val Ala Ala Gly Val Leu Cys Glu Leu Ala Gln Asp
 610 615 620

Lys Glu Ala Ala Glu Ala Ile Glu Ala Glu Gly Ala Thr Ala Pro Leu
 625 630 635 640

Thr Glu Leu Leu His Ser Arg Asn Glu Gly Val Ala Thr Tyr Ala Ala
 645 650 655

Ala Val Leu Phe Arg Met Ser Glu Asp Lys Pro Gln Asp Tyr Lys Lys
 660 665 670

Arg Leu Ser Val Glu Leu Thr Ser Ser Leu Phe Arg Thr Glu Pro Met
 675 680 685

Ala Trp Asn Glu Thr Ala Asp Leu Gly Leu Asp Ile Gly Ala Gln Gly
 690 695 700

Glu Pro Leu Gly Tyr Arg Gln Asp Asp Pro Ser Tyr Arg Ser Phe His
 705 710 715 720

Ser Gly Gly Tyr Gly Gln Asp Ala Leu Gly Met Asp Pro Met Met Glu
 725 730 735

Protein Complexes associated with APP-processing
 His Glu Met Gly Gly His His Pro Gly Ala Asp Tyr Pro Val Asp Gly
 740 745 750

Leu Pro Asp Leu Gly His Ala Gln Asp Leu Met Asp Gly Leu Pro Pro
 755 760 765

Gly Asp Ser Asn Gln Leu Ala Trp Phe Asp Thr Asp Leu
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<211> 179

<212> PRT

<213> Homo sapiens

<400> 5

Met Pro Ser Lys Ser Leu Val Met Glu Tyr Leu Ala His Pro Ser Thr
 1 5 10 15

Leu Gly Leu Ala Val Gly Val Ala Cys Gly Met Cys Leu Gly Trp Ser
 20 25 30

Leu Arg Val Cys Phe Gly Met Leu Pro Lys Ser Lys Thr Ser Lys Thr
 35 40 45

His Thr Asp Thr Glu Ser Glu Ala Ser Ile Leu Gly Asp Ser Gly Glu
 50 55 60

Tyr Lys Met Ile Leu Val Val Arg Asn Asp Leu Lys Met Gly Lys Gly
 65 70 75 80

Lys Val Ala Ala Gln Cys Ser His Ala Ala Val Ser Ala Tyr Lys Gln
 85 90 95

Ile Gln Arg Arg Asn Pro Glu Met Leu Lys Gln Trp Glu Tyr Cys Gly
 100 105 110

Gln Pro Lys Val Val Val Lys Ala Pro Asp Glu Glu Thr Leu Ile Ala
 115 120 125

Leu Leu Ala His Ala Lys Met Leu Gly Leu Thr Val Ser Leu Ile Gln
 130 135 140

Asp Ala Gly Arg Thr Gln Ile Ala Pro Gly Ser Gln Thr Val Leu Gly
 145 150 155 160

Ile Gly Pro Gly Pro Ala Asp Leu Ile Asp Lys Val Thr Gly His Leu
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Protein Complexes associated with APP-processing

Lys Leu Tyr

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Met Lys Glu Asn Tyr Cys Leu Gln Ala Ala Leu Val Cys Leu Gly Met
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Leu Cys His Ser His Ala Phe Ala Pro Glu Arg Arg Gly His Leu Arg
 20 25 30

Pro Ser Phe His Gly His His Glu Lys Gly Lys Glu Gly Gln Val Leu
 35 40 45

Gln Arg Ser Lys Arg Gly Trp Val Trp Asn Gln Phe Phe Val Ile Glu
 50 55 60

Glu Tyr Thr Gly Pro Asp Pro Val Leu Val Gly Arg Leu His Ser Asp
 65 70 75 80

Ile Asp Ser Gly Asp Gly Asn Ile Lys Tyr Ile Leu Ser Gly Glu Gly
 85 90 95

Ala Gly Thr Ile Phe Val Ile Asp Asp Lys Ser Gly Asn Ile His Ala
 100 105 110

Thr Lys Thr Leu Asp Arg Glu Glu Arg Ala Gln Tyr Thr Leu Met Ala
 115 120 125

Gln Ala Val Asp Arg Asp Thr Asn Arg Pro Leu Glu Pro Pro Ser Glu
 130 135 140

Phe Ile Val Lys Val Gln Asp Ile Asn Asp Asn Pro Pro Glu Phe Leu
 145 150 155 160

His Glu Thr Tyr His Ala Asn Val Pro Glu Arg Ser Asn Val Gly Thr
 165 170 175

Ser Val Ile Gln Val Thr Ala Ser Asp Ala Asp Asp Pro Thr Tyr Gly
 180 185 190

Asn Ser Ala Lys Leu Val Tyr Ser Ile Leu Glu Gly Gln Pro Tyr Phe
 195 200 205

Protein Complexes associated with APP-processing

Ser Val Glu Ala Gln Thr Gly Ile Ile Arg Thr Ala Leu Pro Asn Met
 210 215 220

Asp Arg Glu Ala Lys Glu Glu Tyr His Val Val Ile Gln Ala Lys Asp
 225 230 235 240

Met Gly Gly His Met Gly Gly Leu Ser Gly Thr Thr Lys Val Thr Ile
 245 250 255

Thr Leu Thr Asp Val Asn Asp Asn Pro Pro Lys Phe Pro Gln Arg Leu
 260 265 270

Tyr Gln Met Ser Val Ser Glu Ala Ala Val Pro Gly Glu Glu Val Gly
 275 280 285

Arg Val Lys Ala Lys Asp Pro Asp Ile Gly Glu Asn Gly Leu Val Thr
 290 295 300

Tyr Asn Ile Val Asp Gly Asp Gly Met Glu Ser Phe Glu Ile Thr Thr
 305 310 315 320

Asp Tyr Glu Thr Gln Glu Gly Val Ile Lys Leu Lys Lys Pro Val Asp
 325 330 335

Phe Glu Thr Glu Arg Ala Tyr Ser Leu Lys Val Glu Ala Ala Asn Val
 340 345 350

His Ile Asp Pro Lys Phe Ile Ser Asn Gly Pro Phe Lys Asp Thr Val
 355 360 365

Thr Val Lys Ile Ser Val Glu Asp Ala Asp Glu Pro Pro Met Phe Leu
 370 375 380

Ala Pro Ser Tyr Ile His Glu Val Gln Glu Asn Ala Ala Ala Gly Thr
 385 390 395 400

Val Val Gly Arg Val His Ala Lys Asp Pro Asp Ala Ala Asn Ser Pro
 405 410 415

Ile Arg Tyr Ser Ile Asp Arg His Thr Asp Leu Asp Arg Phe Phe Thr
 420 425 430

Ile Asn Pro Glu Asp Gly Phe Ile Lys Thr Thr Lys Pro Leu Asp Arg
 435 440 445

Glu Glu Thr Ala Trp Leu Asn Ile Thr Val Phe Ala Ala Glu Ile His
 450 455 460

Asn Arg His Gln Glu Ala Gln Val Pro Val Ala Ile Arg Val Leu Asp
 465 470 475 480

Protein Complexes associated with APP-processing

Val. Asn Asp Asn Ala Pro Lys Phe Ala Ala Pro Tyr Glu Gly Phe Ile
485 490 495

Cys Glu Ser Asp Gln Thr Lys Pro Leu Ser Asn Gln Pro Ile Val Thr
500 505 510

Ile Ser Ala Asp Asp Lys Asp Asp Thr Ala Asn Gly Pro Arg Phe Ile
515 520 525

Phe Ser Leu Pro Pro Glu Ile Ile His Asn Pro Asn Phe Thr Val Arg
530 535 540

Asp Asn Arg Asp Asn Thr Ala Gly Val Tyr Ala Arg Arg Gly Gly Phe
545 550 555 560

Ser Arg Gln Lys Gln Asp Leu Tyr Leu Leu Pro Ile Val Ile Ser Asp
565 570 575

Gly Gly Ile Pro Pro Met Ser Ser Thr Asn Thr Leu Thr Ile Lys Val
580 585 590

Cys Gly Cys Asp Val Asn Gly Ala Leu Leu Ser Cys Asn Ala Glu Ala
595 600 605

Tyr Ile Leu Asn Ala Gly Leu Ser Thr Gly Ala Leu Ile Ala Ile Leu
610 615 620

Ala Cys Ile Val Ile Leu Leu Val Ile Val Val Leu Phe Val Thr Leu
625 630 635 640

Arg Arg Gln Lys Lys Glu Pro Leu Ile Val Phe Glu Glu Glu Asp Val
645 650 655

Arg Glu Asn Ile Ile Thr Tyr Asp Asp Glu Gly Gly Gly Glu Glu Asp
660 665 670

Thr Glu Ala Phe Asp Ile Ala Thr Leu Gln Asn Pro Asp Gly Ile Asn
675 680 685

Gly Phe Ile Pro Arg Lys Asp Ile Lys Pro Glu Tyr Gln Tyr Met Pro
690 695 700

Arg Pro Gly Leu Arg Pro Ala Pro Asn Ser Val Asp Val Asp Asp Phe
705 710 715 720

Ile Asn Thr Arg Ile Gln Glu Ala Asp Asn Asp Pro Thr Ala Pro Pro
725 730 735

Tyr Asp Ser Ile Gln Ile Tyr Gly Tyr Glu Gly Arg Gly Ser Val Ala
740 745 750

Protein Complexes associated with APP-processing
 Gly Ser Leu Ser Ser Leu Glu Ser Ala Thr Thr Asp Ser Asp Leu Asp
 755 760 765

Tyr Asp Tyr Leu Gln Asn Trp Gly Pro Arg Phe Lys Lys Leu Ala Asp
 770 775 780

Leu Tyr Gly Ser Lys Asp Thr Phe Asp Asp Asp Ser
 785 790 795

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<212> PRT

<213> Homo sapiens

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<223> amino acid

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Thr Gly Val Gly Ala Asp Gln Pro Pro Met Glu Val Phe Ser Ile Asp
 20 25 30

Ser Met Ser Gly Arg Met Tyr Val Thr Arg Pro Met Asp Arg Glu Glu
 35 40 45

His Ala Ser Tyr His Leu Arg Ala His Ala Val Asp Met Asn Gly Asn
 50 55 60

Lys Val Glu Asn Pro Ile Asp Leu Tyr Ile Tyr Val Ile Asp Met Asn
 65 70 75 80

Asp Asn Arg Pro Glu Phe Ile Asn Gln Val Tyr Asn Gly Ser Val Asp
 85 90 95

Protein Complexes associated with APP-processing
 Glu Gly Ser Lys Pro Gly Thr Tyr Val Met Thr Val Thr Ala Asn Asp
 100 105 110

Ala Asp Asp Ser Thr Thr Ala Asn Gly Met Val Arg Tyr Arg Ile Val
 115 120 125

Thr Gln Thr Pro Gln Ser Pro Ser Gln Asn Met Phe Thr Ile Asn Ser
 130 135 140

Glu Thr Gly Asp Ile Val Thr Val Ala Ala Gly Leu Asp Arg Glu Lys
 145 150 155 160

Val Gln Gln Tyr Thr Val Ile Val Gln Ala Thr Asp Met Glu Gly Asn
 165 170 175

Leu Asn Tyr Gly Leu Ser Asn Thr Ala Thr Ala Ile Ile Thr Val Thr
 180 185 190

Asp Val Asn Asp Asn Pro Pro Glu Phe Thr Ala Ser Thr Phe Ala Gly
 195 200 205

Glu Val Pro Glu Asn Arg Val Glu Thr Val Val Ala Asn Leu Thr Val
 210 215 220

Met Asp Arg Asp Gln Pro His Ser Pro Asn Trp Asn Ala Val Tyr Arg
 225 230 235 240

Ile Ile Ser Gly Asp Pro Ser Gly His Phe Ser Val Arg Thr Asp Pro
 245 250 255

Val Thr Asn Glu Gly Met Val Thr Val Val Lys Ala Val Asp Tyr Glu
 260 265 270

Leu Asn Arg Ala Phe Met Leu Thr Val Met Val Ser Asn Gln Ala Pro
 275 280 285

Leu Ala Ser Gly Ile Gln Met Ser Phe Gln Ser Thr Ala Gly Val Thr
 290 295 300

Ile Ser Ile Met Asp Ile Asn Glu Ala Pro Tyr Phe Pro Ser Asn His
 305 310 315 320

Lys Leu Ile Arg Leu Glu Glu Gly Val Pro Pro Gly Thr Val Leu Thr
 325 330 335

Thr Phe Ser Ala Val Asp Pro Asp Arg Phe Met Gln Gln Ala Val Arg
 340 345 350

Tyr Ser Lys Leu Ser Asp Pro Ala Ser Trp Leu His Ile Asn Ala Thr
 355 360 365

Protein Complexes associated with APP-processing

Asn Gly Gln Ile Thr Thr Ala Ala Val Leu Asp Arg Glu Ser Leu Tyr
 370 375 380

Thr Lys Asn Asn Val Tyr Glu Ala Thr Phe Leu Ala Ala Asp Asn Gly
 385 390 395 400

Ile Pro Pro Ala Ser Gly Thr Gly Thr Leu Gln Ile Tyr Leu Ile Asp
 405 410 415

Ile Asn Asp Asn Ala Pro Glu Leu Leu Pro Lys Glu Ala Gln Ile Cys
 420 425 430

Glu Lys Pro Asn Leu Asn Ala Ile Asn Ile Thr Ala Ala Asp Ala Asp
 435 440 445

Val Asp Pro Asn Ile Gly Pro Tyr Val Phe Glu Ala Arg Ala Gly Leu
 450 455 460

Trp Leu Asn Val Tyr Cys Cys Phe Ala Pro Gly Asp Tyr Ala Gln Leu
 465 470 475 480

Ser Leu Arg Ile Leu Tyr Leu Glu Ala Gly Met Tyr Asp Val Pro Ile
 485 490 495

Ile Val Thr Asp Ser Gly Asn Pro Pro Leu Ser Asn Thr Ser Ile Ile
 500 505 510

Lys Val Lys Val Cys Pro Cys Asp Asp Asn Gly Asp Cys Thr Thr Ile
 515 520 525

Gly Ala Val Ala Ala Ala Gly Leu Gly Thr Gly Ala Ile Val Ala Ile
 530 535 540

Leu Ile Cys Ile Leu Ile Leu Leu Thr Met Val Leu Leu Phe Val Met
 545 550 555 560

Trp Met Lys Arg Arg Glu Lys Glu Arg His Thr Lys Gln Leu Leu Ile
 565 570 575

Asp Pro Glu Asp Asp Val Arg Asp Asn Ile Leu Lys Tyr Asp Glu Glu
 580 585 590

Gly Gly Gly Glu Glu Asp Gln Val Arg Leu Arg Pro Ala Pro Ala Ser
 595 600 605

Pro Arg Glu Ala Gly Ser His Val Val Xaa Arg Ala Ala Asp Asn Asp
 610 615 620

Pro Thr Ala Pro Pro Tyr Asp Ser Leu Leu Val Phe Asp Tyr Glu Gly
 625 630 635 640

Protein Complexes associated with APP-processing
 Ser Gly Ser Thr Ala Gly Ser Val Ser Ser Leu Asn Ser Ser Ser Ser
 645 650 655

Gly Asp Gln Asp Tyr Asp Tyr Leu Asn Asp Trp Gly Pro Arg Phe Lys
 660 665 670

Lys Leu Ala Asp Met Tyr Gly Gly Gly
 675 680

<210> 8

<211> 941

<212> PRT

<213> Homo sapiens

<400> 8

Met Asp Asp Ser Glu Val Glu Ser Thr Ala Ser Ile Leu Ala Ser Val
 1 5 10 15

Lys Glu Gln Glu Ala Gln Phe Glu Lys Leu Thr Arg Ala Leu Glu Glu
 20 25 30

Glu Arg Arg His Val Ser Ala Gln Leu Glu Arg Val Arg Val Ser Pro
 35 40 45

Gln Asp Ala Asn Pro Leu Met Ala Asn Gly Thr Leu Thr Arg Arg His
 50 55 60

Gln Asn Gly Arg Phe Val Gly Asp Ala Asp Leu Glu Arg Gln Lys Phe
 65 70 75 80

Ser Asp Leu Lys Leu Asn Gly Pro Gln Asp His Ser His Leu Leu Tyr
 85 90 95

Ser Thr Ile Pro Arg Met Gln Glu Pro Gly Gln Ile Val Glu Thr Tyr
 100 105 110

Thr Glu Glu Asp Pro Glu Gly Ala Met Ser Val Val Ser Val Glu Thr
 115 120 125

Ser Asp Asp Gly Thr Thr Arg Arg Thr Glu Thr Thr Val Lys Lys Val
 130 135 140

Val Lys Thr Val Thr Thr Arg Thr Val Gln Pro Val Ala Met Gly Pro
 145 150 155 160

Asp Gly Leu Pro Val Asp Ala Ser Ser Val Ser Asn Asn Tyr Ile Gln
 165 170 175

Protein Complexes associated with APP-processing

Thr Leu Gly Arg Asp Phe Arg Lys Asn Gly Asn Gly Gly Pro Gly Pro
180 185 190

Tyr Val Gly Gln Ala Gly Thr Ala Thr Leu Pro Arg Asn Phe His Tyr
195 200 205

Pro Pro Asp Gly Tyr Ser Arg His Tyr Glu Asp Gly Tyr Pro Gly Gly
210 215 220

Ser Asp Asn Tyr Gly Ser Leu Ser Arg Val Thr Arg Ile Glu Glu Arg
225 230 235 240

Tyr Arg Pro Ser Met Glu Gly Tyr Arg Ala Pro Ser Arg Gln Asp Val
245 250 255

Tyr Gly Pro Gln Pro Gln Val Arg Val Gly Gly Ser Ser Val Asp Leu
260 265 270

His Arg Phe His Pro Glu Pro Tyr Gly Leu Glu Asp Asp Gln Arg Ser
275 280 285

Met Gly Tyr Asp Asp Leu Asp Tyr Gly Met Met Ser Asp Tyr Gly Thr
290 295 300

Ala Arg Arg Thr Gly Thr Pro Ser Asp Pro Arg Arg Arg Leu Arg Ser
305 310 315 320

Tyr Glu Asp Met Ile Gly Glu Glu Val Pro Ser Asp Gln Tyr Tyr Trp
325 330 335

Ala Pro Leu Ala Gln His Glu Arg Gly Ser Leu Ala Ser Leu Asp Ser
340 345 350

Leu Arg Lys Gly Gly Pro Pro Pro Pro Asn Trp Arg Gln Pro Glu Leu
355 360 365

Pro Glu Val Ile Ala Met Leu Gly Phe Arg Leu Asp Ala Val Lys Ser
370 375 380

Asn Ala Ala Ala Tyr Leu Gln His Leu Cys Tyr Arg Asn Asp Lys Val
385 390 395 400

Lys Thr Asp Val Arg Lys Leu Lys Gly Ile Pro Val Leu Val Gly Leu
405 410 415

Leu Asp His Pro Lys Lys Glu Val His Leu Gly Ala Cys Gly Ala Leu
420 425 430

Lys Asn Ile Ser Phe Gly Arg Asp Gln Asp Asn Lys Ile Ala Ile Lys
435 440 445

Protein Complexes associated with APP-processing

Asn Cys Asp Gly Val Pro Ala Leu Val Arg Leu Leu Arg Lys Ala Arg
 450 455 460

Asp Met Asp Leu Thr Glu Val Ile Thr Gly Thr Leu Trp Asn Leu Ser
 465 470 475 480

Ser His Asp Ser Ile Lys Met Glu Ile Val Asp His Ala Leu His Ala
 485 490 495

Leu Thr Asp Glu Val Ile Ile Pro His Ser Gly Trp Glu Arg Glu Pro
 500 505 510

Asn Glu Asp Cys Lys Pro Arg His Ile Glu Trp Glu Ser Val Leu Thr
 515 520 525

Asn Thr Ala Gly Cys Leu Arg Asn Val Ser Ser Glu Arg Ser Glu Ala
 530 535 540

Arg Arg Lys Leu Arg Glu Cys Asp Gly Leu Val Asp Ala Leu Ile Phe
 545 550 555 560

Ile Val Gln Ala Glu Ile Gly Gln Lys Asp Ser Asp Ser Lys Leu Val
 565 570 575

Glu Asn Cys Val Cys Leu Leu Arg Asn Leu Ser Tyr Gln Val His Arg
 580 585 590

Glu Ile Pro Gln Ala Glu Arg Tyr Gln Glu Ala Ala Pro Asn Val Ala
 595 600 605

Asn Asn Thr Gly Pro His Ala Ala Ser Cys Phe Gly Ala Lys Lys Gly
 610 615 620

Lys Gly Lys Lys Pro Ile Glu Asp Pro Ala Asn Asp Thr Val Asp Phe
 625 630 635 640

Pro Lys Arg Thr Ser Pro Ala Arg Gly Tyr Glu Leu Leu Phe Gln Pro
 645 650 655

Glu Val Val Arg Ile Tyr Ile Ser Leu Leu Lys Glu Ser Lys Thr Pro
 660 665 670

Ala Ile Leu Glu Ala Ser Ala Gly Ala Ile Gln Asn Leu Cys Ala Gly
 675 680 685

Arg Trp Thr Tyr Gly Arg Tyr Ile Arg Ser Ala Leu Arg Gln Glu Lys
 690 695 700

Ala Leu Ser Ala Ile Ala Asp Leu Leu Thr Asn Glu His Glu Arg Val
 705 710 715 720

Protein Complexes associated with APP-processing

Val Lys Ala Ala Ser Gly Ala Leu Arg Asn Leu Ala Val Asp Ala Arg
725 730 735

Asn Lys Glu Leu Ile Gly Lys His Ala Ile Pro Asn Leu Val Lys Asn
740 745 750

Leu Pro Gly Gly Gln Gln Asn Ser Ser Trp Asn Phe Ser Glu Asp Thr
755 760 765

Val Ile Ser Ile Leu Asn Thr Ile Asn Glu Val Ile Ala Glu Asn Leu
770 775 780

Glu Ala Ala Lys Lys Leu Arg Glu Thr Gln Gly Ile Glu Lys Leu Val
785 790 795 800

Leu Ile Asn Lys Ser Gly Asn Arg Ser Glu Lys Glu Val Arg Ala Ala
805 810 815

Ala Leu Val Leu Gln Thr Ile Trp Gly Tyr Lys Glu Leu Arg Lys Pro
820 825 830

Leu Glu Lys Glu Gly Trp Lys Lys Ser Asp Phe Gln Val Asn Leu Asn
835 840 845

Asn Ala Ser Arg Ser Gln Ser Ser His Ser Tyr Asp Asp Ser Thr Leu
850 855 860

Pro Leu Ile Asp Arg Asn Gln Lys Ser Asp Asn Asn Tyr Ser Thr Pro
865 870 875 880

Asn Glu Arg Gly Asp His Asn Arg Thr Leu Asp Arg Ser Gly Asp Leu
885 890 895

Gly Asp Met Glu Pro Leu Lys Gly Thr Thr Pro Leu Met Gln Asp Glu
900 905 910

Gly Gln Glu Ser Leu Glu Glu Glu Leu Asp Val Leu Val Leu Asp Asp
915 920 925

Glu Gly Gly Gln Val Ser Tyr Pro Ser Met Gln Lys Ile
930 935 940

<210> 9

<211> 1225

<212> PRT

<213> Homo sapiens

<400> 9

Protein Complexes associated with APP-processing
 Met Phe Ala Arg Lys Pro Pro Gly Ala Ala Pro Leu Gly Ala Met Pro
 1 5 10 15

Val Pro Asp Gln Pro Ser Ser Ala Ser Glu Lys Thr Ser Ser Leu Ser
 20 25 30

Pro Gly Leu Asn Thr Ser Asn Gly Asp Gly Ser Glu Thr Glu Thr Thr
 35 40 45

Ser Ala Ile Leu Ala Ser Val Lys Glu Gln Glu Leu Gln Phe Glu Arg
 50 55 60

Leu Thr Arg Glu Leu Glu Ala Glu Arg Gln Ile Val Ala Ser Gln Leu
 65 70 75 80

Glu Arg Cys Lys Leu Gly Ser Glu Thr Gly Ser Met Ser Ser Met Ser
 85 90 95

Ser Ala Glu Glu Gln Phe Gln Trp Gln Ser Gln Asp Gly Gln Lys Asp
 100 105 110

Ile Glu Asp Glu Leu Thr Thr Gly Leu Glu Leu Val Asp Ser Cys Ile
 115 120 125

Arg Ser Leu Gln Glu Ser Gly Ile Leu Asp Pro Gln Asp Tyr Ser Thr
 130 135 140

Gly Glu Arg Pro Ser Leu Leu Ser Gln Ser Ala Leu Gln Leu Asn Ser
 145 150 155 160

Lys Pro Glu Gly Ser Phe Gln Tyr Pro Ala Ser Tyr His Ser Asn Gln
 165 170 175

Thr Leu Ala Leu Gly Glu Thr Thr Pro Ser Gln Leu Pro Ala Arg Gly
 180 185 190

Thr Gln Ala Arg Ala Thr Gly Gln Ser Phe Ser Gln Gly Thr Thr Ser
 195 200 205

Arg Ala Gly His Leu Ala Gly Pro Glu Pro Ala Pro Pro Pro Pro Pro
 210 215 220

Pro Pro Arg Glu Pro Phe Ala Pro Ser Leu Gly Ser Ala Phe His Leu
 225 230 235 240

Pro Asp Ala Pro Pro Ala Ala Ala Ala Ala Leu Tyr Tyr Ser Ser
 245 250 255

Ser Thr Leu Pro Ala Pro Pro Arg Gly Gly Ser Pro Leu Ala Ala Pro
 260 265 270

Protein Complexes associated with APP-processing

Gln Gly Gly Ser Pro Thr Lys Leu Gln Arg Gly Gly Ser Ala Pro Glu
 275 280 285

Gly Ala Thr Tyr Ala Ala Pro Arg Gly Ser Ser Pro Lys Gln Ser Pro
 290 295 300

Ser Arg Leu Ala Lys Ser Tyr Ser Thr Ser Ser Pro Ile Asn Ile Val
 305 310 315 320

Val Ser Ser Ala Gly Leu Ser Pro Ile Arg Val Thr Ser Pro Pro Thr
 325 330 335

Val Gln Ser Thr Ile Ser Ser Ser Pro Ile His Gln Leu Ser Ser Thr
 340 345 350

Ile Gly Thr Tyr Ala Thr Leu Ser Pro Thr Lys Arg Leu Val His Ala
 355 360 365

Ser Glu Gln Tyr Ser Lys His Ser Gln Glu Leu Tyr Ala Thr Ala Thr
 370 375 380

Leu Gln Arg Pro Gly Ser Leu Ala Ala Gly Ser Arg Ala Ser Tyr Ser
 385 390 395 400

Ser Gln His Gly His Leu Gly Pro Glu Leu Arg Ala Leu Gln Ser Pro
 405 410 415

Glu His His Ile Asp Pro Ile Tyr Glu Val Arg Val Tyr Gln Lys Pro
 420 425 430

Pro Met Arg Ser Leu Ser Gln Ser Gln Gly Val Pro Leu Pro Pro Ala
 435 440 445

His Thr Gly Thr Tyr Arg Thr Ser Thr Ala Pro Ser Ser Pro Gly Val
 450 455 460

Asp Ser Val Pro Leu Gln Arg Thr Gly Ser Gln His Gly Pro Gln Asn
 465 470 475 480

Ala Ala Ala Ala Thr Phe Gln Arg Ala Ser Tyr Ala Ala Gly Pro Ala
 485 490 495

Ser Asn Tyr Ala Asp Pro Tyr Arg Gln Leu Gln Tyr Cys Pro Ser Val
 500 505 510

Glu Ser Pro Tyr Ser Lys Ser Gly Pro Ala Leu Pro Pro Glu Gly Thr
 515 520 525

Leu Ala Arg Ser Pro Ser Ile Asp Ser Ile Gln Lys Asp Pro Arg Glu
 530 535 540

Protein Complexes associated with APP-processing
 Phe Gly Trp Arg Asp Pro Glu Leu Pro Glu Val Ile Gln Met Leu Gln
 545 550 555 560

His Gln Phe Pro Ser Val Gln Ser Asn Ala Ala Ala Tyr Leu Gln His
 565 570 575

Leu Cys Phe Gly Asp Asn Lys Ile Lys Ala Glu Ile Arg Arg Gln Gly
 580 585 590

Gly Ile Gln Leu Leu Val Asp Leu Leu Asp His Arg Met Thr Glu Val
 595 600 605

His Arg Ser Ala Cys Gly Ala Leu Arg Asn Leu Val Tyr Gly Lys Ala
 610 615 620

Asn Asp Asp Asn Lys Ile Ala Leu Lys Asn Cys Gly Gly Ile Pro Ala
 625 630 635 640

Leu Val Arg Leu Leu Arg Lys Thr Thr Asp Leu Glu Ile Arg Glu Leu
 645 650 655

Val Thr Gly Val Leu Trp Asn Leu Ser Ser Cys Asp Ala Leu Lys Met
 660 665 670

Pro Ile Ile Gln Asp Ala Leu Ala Val Leu Thr Asn Ala Val Ile Ile
 675 680 685

Pro His Ser Gly Trp Glu Asn Ser Pro Leu Gln Asp Asp Arg Lys Ile
 690 695 700

Gln Leu His Ser Ser Gln Val Leu Arg Asn Ala Thr Gly Cys Leu Arg
 705 710 715 720

Asn Val Ser Ser Pro Gly Glu Glu Ala Arg Arg Arg Met Arg Glu Cys
 725 730 735

Asp Gly Leu Thr Asp Ala Leu Leu Tyr Val Ile Gln Ser Ala Leu Gly
 740 745 750

Ser Ser Glu Ile Asp Ser Lys Thr Val Glu Asn Cys Val Cys Ile Leu
 755 760 765

Arg Asn Leu Ser Tyr Arg Leu Ala Ala Glu Thr Ser Gln Gly Gln His
 770 775 780

Met Gly Thr Asp Glu Leu Asp Gly Leu Leu Cys Gly Glu Ala Asn Gly
 785 790 795 800

Lys Asp Ala Glu Ser Ser Gly Cys Trp Gly Lys Lys Lys Lys Lys
 805 810 815

Protein Complexes associated with APP-processing

Lys Ser Gln Asp Gln Trp Asp Gly Val Gly Pro Leu Pro Asp Cys Ala
 820 825 830

Glu Pro Pro Lys Gly Ile Gln Met Leu Trp His Pro Ser Ile Val Lys
 835 840 845

Pro Tyr Leu Thr Leu Leu Ser Glu Cys Ser Asn Pro Asp Thr Leu Glu
 850 855 860

Gly Ala Ala Gly Ala Leu Gln Asn Leu Ala Ala Gly Ser Trp Lys Trp
 865 870 875 880

Ser Val Tyr Ile Arg Ala Ala Val Arg Lys Glu Lys Gly Arg Pro Ile
 885 890 895

Leu Val Glu Leu Leu Arg Ile Asp Asn Asp Arg Val Ala Cys Ala Val
 900 905 910

Ala Thr Ala Leu Arg Asn Met Ala Leu Asp Val Arg Asn Lys Glu Leu
 915 920 925

Ile Gly Lys Tyr Ala Met Arg Asp Leu Val His Arg Leu Pro Gly Gly
 930 935 940

Asn Asn Ser Asn Asn Thr Ala Ser Lys Ala Met Ser Asp Asp Thr Val
 945 950 955 960

Thr Ala Val Cys Cys Thr Leu His Glu Val Ile Thr Lys Asn Met Glu
 965 970 975

Asn Ala Lys Ala Leu Arg Asp Ala Gly Gly Ile Glu Lys Leu Val Gly
 980 985 990

Ile Ser Lys Ser Lys Gly Asp Lys His Ser Pro Lys Val Val Lys Ala
 995 1000 1005

Ala Ser Gln Val Leu Asn Ser Met Trp Gln Tyr Arg Asp Leu Arg
 1010 1015 1020

Ser Leu Tyr Lys Lys Asp Gly Trp Ser Gln Tyr His Phe Val Ala
 1025 1030 1035

Ser Ser Ser Thr Ile Glu Arg Asp Arg Gln Arg Pro Tyr Ser Ser
 1040 1045 1050

Ser Arg Thr Pro Ser Ile Ser Pro Val Arg Val Ser Pro Asn Asn
 1055 1060 1065

Arg Ser Ala Ser Ala Pro Ala Ser Pro Arg Glu Met Ile Ser Leu
 1070 1075 1080

Protein Complexes associated with APP-processing

Lys Glu Arg Lys Thr Asp Tyr Glu Cys Thr Gly Ser Asn Ala Thr
 1085 1090 1095

Tyr His Gly Ala Lys Gly Glu His Thr Ser Arg Lys Asp Ala Met
 1100 1105 1110

Thr Ala Gln Asn Thr Gly Ile Ser Thr Leu Tyr Arg Asn Ser Tyr
 1115 1120 1125

Gly Ala Pro Ala Glu Asp Ile Lys His Asn Gln Val Ser Ala Gln
 1130 1135 1140

Pro Val Pro Gln Glu Pro Ser Arg Lys Asp Tyr Glu Thr Tyr Gln
 1145 1150 1155

Pro Phe Gln Asn Ser Thr Arg Asn Tyr Asp Glu Ser Phe Phe Glu
 1160 1165 1170

Asp Gln Val His His Arg Pro Pro Ala Ser Glu Tyr Thr Met His
 1175 1180 1185

Leu Gly Leu Lys Ser Thr Gly Asn Tyr Val Asp Phe Tyr Ser Ala
 1190 1195 1200

Ala Arg Pro Tyr Ser Glu Leu Asn Tyr Glu Thr Ser His Tyr Pro
 1205 1210 1215

Ala Ser Pro Asp Ser Trp Val
 1220 1225

<210> 10

<211> 495

<212> PRT

<213> Homo sapiens

<400> 10

Met Arg Leu Thr Arg Cys Gln Ala Ala Leu Ala Ala Ala Ile Thr Leu
 1 5 10 15

Asn Leu Leu Val Leu Phe Tyr Val Ser Trp Leu Gln His Gln Pro Arg
 20 25 30

Asn Ser Arg Ala Arg Gly Pro Arg Arg Ala Ser Ala Ala Gly Pro Arg
 35 40 45

Val Thr Val Leu Val Arg Glu Phe Glu Ala Phe Asp Asn Ala Val Pro
 50 55 60

Protein Complexes associated with APP-processing

Glu Leu Val Asp Ser Phe Leu Gln Gln Asp Pro Ala Gln Pro Val Val
 65 70 75 80

Val Ala Ala Asp Thr Leu Pro Tyr Pro Pro Leu Ala Leu Pro Arg Ile
 85 90 95

Pro Asn Val Arg Leu Ala Leu Leu Gln Pro Ala Leu Asp Arg Pro Ala
 100 105 110

Ala Ala Ser Arg Pro Glu Thr Tyr Val Ala Thr Glu Phe Val Ala Leu
 115 120 125

Val Pro Asp Gly Ala Arg Ala Glu Ala Pro Gly Leu Leu Glu Arg Met
 130 135 140

Val Glu Ala Leu Arg Ala Gly Ser Ala Arg Leu Val Ala Ala Pro Val
 145 150 155 160

Ala Thr Ala Asn Pro Ala Arg Cys Leu Ala Leu Asn Val Ser Leu Arg
 165 170 175

Glu Trp Thr Ala Arg Tyr Gly Ala Ala Pro Ala Ala Pro Arg Cys Asp
 180 185 190

Ala Leu Asp Gly Asp Ala Val Val Leu Leu Arg Ala Arg Asp Leu Phe
 195 200 205

Asn Leu Ser Ala Pro Leu Ala Arg Pro Val Gly Thr Ser Leu Phe Leu
 210 215 220

Gln Thr Ala Leu Arg Gly Trp Ala Val Gln Leu Leu Asp Leu Thr Phe
 225 230 235 240

Ala Ala Ala Arg Gln Pro Pro Leu Ala Thr Ala His Ala Arg Trp Lys
 245 250 255

Ala Glu Arg Glu Gly Arg Ala Arg Arg Ala Ala Leu Leu Arg Ala Leu
 260 265 270

Gly Ile Arg Leu Val Ser Trp Glu Gly Gly Arg Leu Glu Trp Phe Gly
 275 280 285

Cys Asn Lys Glu Thr Thr Arg Cys Phe Gly Thr Val Val Gly Asp Thr
 290 295 300

Pro Ala Tyr Leu Tyr Glu Glu Arg Trp Thr Pro Pro Cys Cys Leu Arg
 305 310 315 320

Ala Leu Arg Glu Thr Ala Arg Tyr Val Val Gly Val Leu Glu Ala Ala
 325 330 335

Protein Complexes associated with APP-processing

Gly Val Arg Tyr Trp Leu Glu Gly Ser Leu Leu Gly Ala Ala Arg
 340 345 350

His Gly Asp Ile Ile Pro Trp Asp Tyr Asp Val Asp Leu Gly Ile Tyr
 355 360 365

Leu Glu Asp Val Gly Asn Cys Glu Gln Leu Arg Gly Ala Glu Ala Gly
 370 375 380

Ser Val Val Asp Glu Arg Gly Phe Val Trp Glu Lys Ala Val Glu Gly
 385 390 395 400

Asp Phe Phe Arg Val Gln Tyr Ser Glu Ser Asn His Leu His Val Asp
 405 410 415

Leu Trp Pro Phe Tyr Pro Arg Asn Gly Val Met Thr Lys Asp Thr Trp
 420 425 430

Leu Asp His Arg Gln Asp Val Glu Phe Pro Glu His Phe Leu Gln Pro
 435 440 445

Leu Val Pro Leu Pro Phe Ala Gly Phe Val Ala Gln Ala Pro Asn Asn
 450 455 460

Tyr Arg Arg Phe Leu Glu Leu Lys Phe Gly Pro Gly Val Ile Glu Asn
 465 470 475 480

Pro Gln Tyr Pro Asn Pro Ala Leu Leu Ser Leu Thr Gly Ser Gly
 485 490 495

<210> 11

<211> 449

<212> PRT

<213> Homo sapiens

<400> 11

Met Pro Ala Thr Leu Leu Arg Ala Val Ala Arg Ser His His Ile Leu
 1 5 10 15

Ser Lys Ala His Gln Cys Arg Arg Ile Gly His Leu Met Leu Lys Pro
 20 25 30

Leu Lys Glu Phe Glu Asn Thr Thr Cys Ser Thr Leu Thr Ile Arg Gln
 35 40 45

Ser Leu Asp Leu Phe Leu Pro Asp Lys Thr Ala Ser Gly Leu Asn Lys
 50 55 60

Protein Complexes associated with APP-processing
 Ser Gln Ile Leu Glu Met Asn Gln Lys Lys Ser Asp Thr Ser Met Leu
 65 70 75 80

Ser Pro Leu Asn Ala Ala Arg Cys Gln Asp Glu Lys Ala His Leu Pro
 85 90 95

Thr Met Lys Ser Phe Gly Thr His Arg Arg Val Thr His Lys Pro Asn
 100 105 110

Leu Leu Gly Ser Lys Trp Phe Ile Lys Ile Leu Lys Arg His Phe Ser
 115 120 125

Ser Val Ser Met Glu Thr Phe Val Pro Lys Gln Asp Phe Pro Gln Val
 130 135 140

Lys Arg Pro Leu Lys Ala Ser Arg Thr Arg Gln Pro Ser Arg Thr Asn
 145 150 155 160

Leu Pro Val Leu Ser Val Asn Glu Asp Pro Met His Cys Thr Ala Phe
 165 170 175

Ala Thr Ala Asp Glu Tyr His Leu Gly Asn Leu Ser Gln Asp Leu Ala
 180 185 190

Ser His Gly Tyr Val Glu Val Thr Ser Leu Pro Arg Asp Ala Ala Asn
 195 200 205

Ile Leu Val Met Gly Val Glu Asn Ser Ala Lys Glu Gly Asp Pro Gly
 210 215 220

Thr Ile Phe Phe Phe Arg Glu Gly Ala Ala Val Phe Trp Asn Val Lys
 225 230 235 240

Asp Lys Thr Met Lys His Val Met Lys Val Leu Glu Lys His Glu Ile
 245 250 255

Gln Pro Tyr Glu Ile Ala Leu Val His Trp Glu Asn Glu Glu Leu Asn
 260 265 270

Tyr Ile Lys Ile Glu Gly Gln Ser Lys Leu His Arg Gly Glu Ile Lys
 275 280 285

Leu Asn Ser Glu Leu Asp Leu Asp Asp Ala Ile Leu Glu Lys Phe Ala
 290 295 300

Phe Ser Asn Ala Leu Cys Leu Ser Val Lys Leu Ala Ile Trp Glu Ala
 305 310 315 320

Ser Leu Asp Lys Phe Ile Glu Ser Ile Gln Ser Ile Pro Glu Ala Leu
 325 330 335

Protein Complexes associated with APP-processing
 Lys Ala Gly Lys Lys Val Lys Leu Ser His Glu Glu Val Met Gln Lys
 340 345 350

Ile Gly Glu Leu Phe Ala Leu Arg His Arg Ile Asn Leu Ser Ser Asp
 355 360 365

Phe Leu Ile Thr Pro Asp Phe Tyr Trp Asp Arg Glu Asn Leu Glu Gly
 370 375 380

Leu Tyr Asp Lys Thr Cys Gln Phe Leu Ser Ile Gly Arg Arg Val Lys
 385 390 395 400

Val Met Asn Glu Lys Leu Gln His Cys Met Glu Leu Thr Asp Leu Met
 405 410 415

Arg Asn His Leu Asn Glu Lys Arg Ala Leu Arg Leu Glu Trp Met Ile
 420 425 430

Val Ile Leu Ile Thr Ile Glu Val Met Phe Glu Leu Gly Arg Val Phe
 435 440 445

Phe

<210> 12

<211> 743

<212> PRT

<213> Homo sapiens

<400> 12

Glu Val Met Asn Leu Met Glu Gln Pro Ile Lys Val Thr Glu Trp Gln
 1 5 10 15

Gln Thr Tyr Thr Tyr Asp Ser Gly Ile His Ser Gly Ala Asn Thr Cys
 20 25 30

Val Pro Ser Val Ser Ser Lys Gly Ile Met Glu Glu Asp Glu Ala Cys
 35 40 45

Gly Arg Gln Tyr Thr Leu Lys Lys Thr Thr Thr Tyr Thr Gln Gly Val
 50 55 60

Pro Pro Ser Gln Gly Asp Leu Glu Tyr Gln Met Ser Thr Thr Ala Arg
 65 70 75 80

Ala Lys Arg Val Arg Glu Ala Met Cys Pro Gly Val Ser Gly Glu Gly
 85 90 95

Protein Complexes associated with APP-processing

Gln	Leu	Ala	Leu	Leu	Ala	Thr	Gln	Val	Glu	Gly	Gln	Ala	Thr	Asn	Leu
			100					105						110	

Leu Ile Asn Tyr Gln Asp Asp Ala Glu Leu Val Thr Arg Ala Leu Pro
130 135 140

Ala Ala Met Ile Val Asn Gln Leu Ser Lys Lys Glu Ala Ser Arg Arg
165 170 175

Gln Asn Thr Ser Asp Leu Asp Thr Ala Arg Cys Thr Thr Ser Ile Leu
195 200 205

Gly Gly Ile Pro Ala Leu Val Arg Met Leu Ser Ser Pro Val Glu Ser
225 230 235 240

Glu Gly Ala Lys Met Ala Cys Ala Gly Arg Arg Ala Gln Lys Met Val
260 265 270

Cys Leu Gln Leu Leu Ala Tyr Gly Asn Gln Glu Ser Lys Leu Ile Ile
290 295 300

Ser Tyr Glu Lys Leu Leu Trp Thr Thr Ser Arg Val Leu Lys Val Leu
325 330 335

Gln Ala Leu Gly Lys His Leu Thr Ser Asn Ser Pro Arg Leu Val Gln
355 360 365

Protein Complexes associated with APP-processing

Asn Cys Leu Trp Thr Leu Arg Asn Leu Ser Asp Val Ala Thr Lys Gln
 370 375 380

Glu Gly Leu Glu Ser Val Leu Lys Ile Leu Val Asn Gln Leu Ser Val
 385 390 400

Asp Asp Val Asn Val Leu Thr Cys Ala Thr Gly Thr Leu Ser Asn Leu
 405 410 415

Thr Cys Asn Asn Ser Lys Asn Lys Thr Leu Val Thr Gln Asn Ser Gly
 420 425 430

Val Glu Ala Leu Ile His Ala Ile Leu Arg Ala Gly Asp Lys Asp Asp
 435 440 445

Ile Thr Glu Pro Ala Val Cys Ala Leu Arg His Leu Thr Ser Arg His
 450 455 460

Pro Glu Ala Glu Met Ala Gln Asn Ser Val Arg Leu Asn Tyr Gly Ile
 465 470 475 480

Pro Ala Ile Val Lys Leu Leu Asn Gln Pro Asn Gln Trp Pro Leu Val
 485 490 495

Lys Ala Thr Ile Gly Leu Ile Arg Asn Leu Ala Leu Cys Pro Ala Asn
 500 505 510

His Ala Pro Leu Gln Glu Ala Ala Val Ile Pro Arg Leu Val Gln Leu
 515 520 525

Leu Val Lys Ala His Gln Asp Ala Gln Arg His Val Ala Ala Gly Thr
 530 535 540

Gln Gln Pro Tyr Thr Asp Gly Val Arg Met Glu Glu Ile Val Glu Gly
 545 550 555 560

Cys Thr Gly Ala Leu His Ile Leu Ala Arg Asp Pro Met Asn Arg Met
 565 570 575

Glu Ile Phe Arg Leu Asn Thr Ile Pro Leu Phe Val Gln Leu Leu Tyr
 580 585 590

Ser Ser Val Glu Asn Ile Gln Arg Val Ala Ala Gly Val Leu Cys Glu
 595 600 605

Leu Ala Gln Asp Lys Glu Ala Ala Asp Ala Ile Asp Ala Glu Gly Ala
 610 615 620

Ser Ala Pro Leu Met Glu Leu Leu His Ser Arg Asn Glu Gly Thr Ala
 625 630 635 640

Protein Complexes associated with APP-processing

Protein Complexes associated with APP-processing

Thr Tyr Ala Ala Ala Val Leu Phe Arg Ile Ser Glu Asp Lys Asn Pro
645 650 655

Asp Tyr Arg Lys Arg Val Ser Val Glu Leu Thr Asn Ser Leu phe Lys
660 665 670

His Asp Pro Ala Ala Trp Glu Ala Ala Gln Ser Met Ile Pro Ile Asn
675 680 685

Glu Pro Tyr Gly Asp Asp Met Asp Ala Thr Tyr Arg Pro Met Tyr Ser
690 695 700

Ser 705 Asp Val Pro Leu Asp 710 Pro Leu Glu Met His 715 Met Asp Met Asp Gly 720

Asp Tyr Pro Ile Asp Thr Tyr Ser Asp Gly Leu Arg Pro Pro Tyr Pro
725 730 735

Thr Ala Asp His Met Leu Ala
740

<210> 13

<211> 246

<212> PRT

<213> Homo sapiens

<400> 13

Met Thr Leu Ile Glu Gly Val Gly Asp Glu Val Thr Val Leu Phe Ser
1 5 10 15

Val Leu Ala Cys Leu Leu Val Leu Ala Leu Ala Trp Val Ser Thr His
20 25 30

Thr Ala Glu Gly Gly Asp Pro Leu Pro Gln Pro Ser Gly Thr Pro Thr
35 40 45

Pro Ser Gln Pro Ser Ala Ala Met Ala Ala Thr Asp Ser Met Arg Gly
50 55 60

Glu Ala Pro Gly Ala Glu Thr Pro Ser Leu Arg His Arg Gly Gln Ala
65 70 75 80

Ala Gln Pro Glu Pro Ser Thr Gly Phe Thr Ala Thr Pro Pro Ala Pro
85 90 95

Asp Ser Pro **Gln** Glu Pro Leu Val **Leu** Arg Leu Lys Phe **Leu** Asn Asp
100 105 110

Protein Complexes associated with APP-processing
 Ser Glu Gln Val Ala Arg Ala Trp Pro His Asp Thr Ile Gly Ser Leu
 115 120 125

Lys Arg Thr Gln Phe Pro Gly Arg Glu Gln Gln Val Arg Leu Ile Tyr
 130 135 140

Gln Gly Gln Leu Leu Gly Asp Asp Thr Gln Thr Leu Gly Ser Leu His
 145 150 155 160

Leu Pro Pro Asn Cys Val Leu His Cys His Val Ser Thr Arg Val Gly
 165 170 175

Pro Pro Asn Pro Pro Cys Pro Pro Gly Ser Glu Pro Gly Pro Ser Gly
 180 185 190

Leu Glu Ile Gly Ser Leu Leu Leu Pro Leu Leu Leu Leu Leu Leu Leu
 195 200 205

Leu Leu Trp Tyr Cys Gln Ile Gln Tyr Arg Pro Phe Phe Pro Leu Thr
 210 215 220

Ala Thr Leu Gly Leu Ala Gly Phe Thr Leu Leu Leu Ser Leu Leu Ala
 225 230 235 240

Phe Ala Met Tyr Arg Pro
 245

<210> 14

<211> 709

<212> PRT

<213> Homo sapiens

<400> 14

Met Ala Thr Ala Gly Gly Gly Ser Gly Ala Asp Pro Gly Ser Arg Gly
 1 5 10 15

Leu Leu Arg Leu Leu Ser Phe Cys Val Leu Leu Ala Gly Leu Cys Arg
 20 25 30

Gly Asn Ser Val Glu Arg Lys Ile Tyr Ile Pro Leu Asn Lys Thr Ala
 35 40 45

Pro Cys Val Arg Leu Leu Asn Ala Thr His Gln Ile Gly Cys Gln Ser
 50 55 60

Ser Ile Ser Gly Asp Thr Gly Val Ile His Val Val Glu Lys Glu Glu
 65 70 75 80

Protein Complexes associated with APP-processing

Asp Leu Gln Trp Val Leu Thr Asp Gly Pro Asn Pro Pro Tyr Met Val
85 90 95

Leu Leu Glu Ser Lys His Phe Thr Arg Asp Leu Met Glu Lys Leu Lys
100 105 110

Gly Arg Thr Ser Arg Ile Ala Gly Leu Ala Val Ser Leu Thr Lys Pro
115 120 125

Ser Pro Ala Ser Gly Phe Ser Pro Ser Val Gln Cys Pro Asn Asp Gly
130 135 140

Phe Gly Val Tyr Ser Asn Ser Tyr Gly Pro Glu Phe Ala His Cys Arg
145 150 155 160

Glu Ile Gln Trp Asn Ser Leu Gly Asn Gly Leu Ala Tyr Glu Asp Phe
165 170 175

Ser Phe Pro Ile Phe Leu Leu Glu Asp Glu Asn Glu Thr Lys Val Ile
180 185 190

Lys Gln Cys Tyr Gln Asp His Asn Leu Ser Gln Asn Gly Ser Ala Pro
195 200 205

Thr Phe Pro Leu Cys Ala Met Gln Leu Phe Ser His Met His Ala Val
210 215 220

Ile Ser Thr Ala Thr Cys Met Arg Arg Ser Ser Ile Gln Ser Thr Phe
225 230 235 240

Ser Ile Asn Pro Glu Ile Val Cys Asp Pro Leu Ser Asp Tyr Asn Val
245 250 255

Trp Ser Met Leu Lys Pro Ile Asn Thr Thr Gly Thr Leu Lys Pro Asp
260 265 270

Asp Arg Val Val Val Ala Ala Thr Arg Leu Asp Ser Arg Ser Phe Phe
275 280 285

Trp Asn Val Ala Pro Gly Ala Glu Ser Ala Val Ala Ser Phe Val Thr
290 295 300

Gln Leu Ala Ala Ala Glu Ala Leu Gln Lys Ala Pro Asp Val Thr Thr
305 310 315 320

Leu Pro Arg Asn Val Met Phe Val Phe Phe Gln Gly Glu Thr Phe Asp
325 330 335

Tyr Ile Gly Ser Ser Arg Met Val Tyr Asp Met Glu Lys Gly Lys Phe
340 345 350

Protein Complexes associated with APP-processing

Pro Val Gln Leu Glu Asn Val Asp Ser Phe Val Glu Leu Gly Gln Val
355 360 365

Ala Leu Arg Thr Ser Leu Glu Leu Trp Met His Thr Asp Pro Val Ser
370 375 380

Gln Lys Asn Glu Ser Val Arg Asn Gln Val Glu Asp Leu Leu Ala Thr
385 390 395 400

Leu Glu Lys Ser Gly Ala Gly Val Pro Ala Val Ile Leu Arg Arg Pro
405 410 415

Asn Gln Ser Gln Pro Leu Pro Pro Ser Ser Leu Gln Arg Phe Leu Arg
420 425 430

Ala Arg Asn Ile Ser Gly Val Val Leu Ala Asp His Ser Gly Ala Phe
435 440 445

His Asn Lys Tyr Tyr Gln Ser Ile Tyr Asp Thr Ala Glu Asn Ile Asn
450 455 460

Val Ser Tyr Pro Glu Trp Leu Ser Pro Glu Glu Asp Leu Asn Phe Val
465 470 475 480

Thr Asp Thr Ala Lys Ala Leu Ala Asp Val Ala Thr Val Leu Gly Arg
485 490 495

Ala Leu Tyr Glu Leu Ala Gly Gly Thr Asn Phe Ser Asp Thr Val Gln
500 505 510

Ala Asp Pro Gln Thr Val Thr Arg Leu Leu Tyr Gly Phe Leu Ile Lys
515 520 525

Ala Asn Asn Ser Trp Phe Gln Ser Ile Leu Arg Gln Asp Leu Arg Ser
530 535 540

Tyr Leu Gly Asp Gly Pro Leu Gln His Tyr Ile Ala Val Ser Ser Pro
545 550 555 560

Thr Asn Thr Thr Tyr Val Val Gln Tyr Ala Leu Ala Asn Leu Thr Gly
565 570 575

Thr Val Val Asn Leu Thr Arg Glu Gln Cys Gln Asp Pro Ser Lys Val
580 585 590

Pro Ser Glu Asn Lys Asp Leu Tyr Glu Tyr Ser Trp Val Gln Gly Pro
595 600 605

Leu His Ser Asn Glu Thr Asp Arg Leu Pro Arg Cys Val Arg Ser Thr
610 615 620

Protein Complexes associated with APP-processing
 Ala Arg Leu Ala Arg Ala Leu Ser Pro Ala Phe Glu Leu Ser Gln Trp
 625 630 635 640

Ser Ser Thr Glu Tyr Ser Thr Trp Thr Glu Ser Arg Trp Lys Asp Ile
 645 650 655

Arg Ala Arg Ile Phe Leu Ile Ala Ser Lys Glu Leu Glu Leu Ile Thr
 660 665 670

Leu Thr Val Gly Phe Gly Ile Leu Ile Phe Ser Leu Ile Val Thr Tyr
 675 680 685

Cys Ile Asn Ala Lys Ala Asp Val Leu Phe Ile Ala Pro Arg Glu Pro
 690 695 700

Gly Ala Val Ser Tyr
 705

<210> 15

<211> 101

<212> PRT

<213> Homo sapiens

<400> 15

Met Asn Leu Glu Arg Val Ser Asn Glu Glu Lys Leu Asn Leu Cys Arg
 1 5 10 15

Lys Tyr Tyr Leu Gly Gly Phe Ala Phe Leu Pro Phe Leu Trp Leu Val
 20 25 30

Asn Ile Phe Trp Phe Phe Arg Glu Ala Phe Leu Val Pro Ala Tyr Thr
 35 40 45

Glu Gln Ser Gln Ile Lys Gly Tyr Val Trp Arg Ser Ala Val Gly Phe
 50 55 60

Leu Phe Trp Val Ile Val Leu Thr Ser Trp Ile Thr Ile Phe Gln Ile
 65 70 75 80

Tyr Arg Pro Arg Trp Gly Ala Leu Gly Asp Tyr Leu Ser Phe Thr Ile
 85 90 95

Pro Leu Gly Thr Pro
 100

<210> 16

<211> 1211

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 16

Met Pro Ala Pro Glu Gln Ala Ser Leu Val Glu Glu Gly Gln Pro Gln
 1 5 10 15

Thr Arg Gln Glu Ala Ala Ser Thr Gly Pro Gly Met Glu Pro Glu Thr
 20 25 30

Thr Ala Thr Thr Ile Leu Ala Ser Val Lys Glu Gln Glu Leu Gln Phe
 35 40 45

Gln Arg Leu Thr Arg Glu Leu Glu Val Glu Arg Gln Ile Val Ala Ser
 50 55 60

Gln Leu Glu Arg Cys Arg Leu Gly Ala Glu Ser Pro Ser Ile Ala Ser
 65 70 75 80

Thr Ser Ser Thr Glu Lys Ser Phe Pro Trp Arg Ser Thr Asp Val Pro
 85 90 95

Asn Thr Gly Val Ser Lys Pro Arg Val Ser Asp Ala Val Gln Pro Asn
 100 105 110

Asn Tyr Leu Ile Arg Thr Glu Pro Glu Gln Gly Thr Leu Tyr Ser Pro
 115 120 125

Glu Gln Thr Ser Leu His Glu Ser Glu Gly Ser Leu Gly Asn Ser Arg
 130 135 140

Ser Ser Thr Gln Met Asn Ser Tyr Ser Asp Ser Gly Tyr Gln Glu Ala
 145 150 155 160

Gly Ser Phe His Asn Ser Gln Asn Val Ser Lys Ala Asp Asn Arg Gln
 165 170 175

Gln His Ser Phe Ile Gly Ser Thr Asn Asn His Val Val Arg Asn Ser
 180 185 190

Arg Ala Glu Gly Gln Thr Leu Val Gln Pro Ser Val Ala Asn Arg Ala
 195 200 205

Met Arg Arg Val Ser Ser Val Pro Ser Arg Ala Gln Ser Pro Ser Tyr
 210 215 220

Val Ile Ser Thr Gly Val Ser Pro Ser Arg Gly Ser Leu Arg Thr Ser
 225 230 235 240

Protein Complexes associated with APP-processing

Leu Gly Ser Gly Phe Gly Ser Pro Ser Val Thr Asp Pro Arg Pro Leu
245 250 255

Asn Pro Ser Ala Tyr Ser Ser Thr Thr Leu Pro Ala Ala Arg Ala Ala
260 265 270

Ser Pro Tyr Ser Gln Arg Pro Ala Ser Pro Thr Ala Ile Arg Arg Ile
275 280 285

Gly Ser Val Thr Ser Arg Gln Thr Ser Asn Pro Asn Gly Pro Thr Pro
290 295 300

Gln Tyr Gln Thr Thr Ala Arg Val Gly Ser Pro Leu Thr Leu Thr Asp
305 310 315 320

Ala Gln Thr Arg Val Ala Ser Pro Ser Gln Gly Gln Val Gly Ser Ser
325 330 335

Ser Pro Lys Arg Ser Gly Met Thr Ala Val Pro Gln His Leu Gly Pro
340 345 350

Ser Leu Gln Arg Thr Val His Asp Met Glu Gln Phe Gly Gln Gln Gln
355 360 365

Tyr Asp Ile Tyr Glu Arg Met Val Pro Pro Arg Pro Asp Ser Leu Thr
370 375 380

Gly Leu Arg Ser Ser Tyr Ala Ser Gln His Ser Gln Leu Gly Gln Asp
385 390 395 400

Leu Arg Ser Ala Val Ser Pro Asp Leu His Ile Thr Pro Ile Tyr Glu
405 410 415

Gly Arg Thr Tyr Tyr Ser Pro Val Tyr Arg Ser Pro Asn His Gly Thr
420 425 430

Val Glu Leu Gln Gly Ser Gln Thr Ala Leu Tyr Arg Thr Gly Val Ser
435 440 445

Gly Ile Gly Asn Leu Gln Arg Thr Ser Ser Gln Arg Ser Thr Leu Thr
450 455 460

Tyr Gln Arg Asn Asn Tyr Ala Leu Asn Thr Thr Ala Thr Tyr Ala Glu
465 470 475 480

Pro Tyr Arg Pro Ile Gln Tyr Arg Val Gln Glu Cys Asn Tyr Asn Arg
485 490 495

Leu Gln His Ala Val Pro Ala Asp Asp Gly Thr Thr Arg Ser Pro Ser
500 505 510

Protein Complexes associated with APP-processing

Ile Asp Ser Ile Gln Lys Asp Pro Arg Glu Phe Ala Trp Arg Asp Pro
515 520 525

Glu Leu Pro Glu Val Ile His Met Leu Glu His Gln Phe Pro Ser Val
530 535 540

Gln Ala Asn Ala Ala Ala Tyr Leu Gln His Leu Cys Phe Gly Asp Asn
545 550 555 560

Lys Val Lys Met Glu Val Cys Arg Leu Gly Gly Ile Lys His Leu Val
565 570 575

Asp Leu Leu Asp His Arg Val Leu Glu Val Gln Lys Asn Ala Cys Gly
580 585 590

Ala Leu Arg Asn Leu Val Phe Gly Lys Ser Thr Asp Glu Asn Lys Ile
595 600 605

Ala Met Lys Asn Val Gly Gly Ile Pro Ala Leu Leu Arg Leu Leu Arg
610 615 620

Lys Ser Ile Asp Ala Glu Val Arg Glu Leu Val Thr Gly Val Leu Trp
625 630 635 640

Asn Leu Ser Ser Cys Asp Ala Val Lys Met Thr Ile Ile Arg Asp Ala
645 650 655

Leu Ser Thr Leu Thr Asn Thr Val Ile Val Pro His Ser Gly Trp Asn
660 665 670

Asn Ser Ser Phe Asp Asp Asp His Lys Ile Lys Phe Gln Thr Ser Leu
675 680 685

Val Leu Arg Asn Thr Thr Gly Cys Leu Arg Asn Leu Thr Ser Ala Gly
690 695 700

Glu Glu Ala Arg Lys Gln Met Arg Ser Cys Glu Gly Leu Val Asp Ser
705 710 715 720

Leu Leu Tyr Val Ile His Thr Cys Val Asn Thr Ser Asp Tyr Asp Ser
725 730 735

Lys Thr Val Glu Asn Cys Val Cys Thr Leu Arg Asn Leu Ser Tyr Arg
740 745 750

Leu Glu Leu Glu Val Pro Gln Ala Arg Leu Leu Gly Leu Asn Glu Leu
755 760 765

Asp Asp Leu Leu Gly Lys Glu Ser Pro Ser Lys Asp Ser Glu Pro Ser
770 775 780

Protein Complexes associated with APP-processing

Cys Trp Gly Lys Lys Lys Lys Lys Lys Arg Thr Pro Gln Glu Asp
 785 790 795 800
 Gln Trp Asp Gly Val Gly Pro Ile Pro Gly Leu Ser Lys Ser Pro Lys
 805 810 815
 Gly Val Glu Met Leu Trp His Pro Ser Val Val Lys Pro Tyr Leu Thr
 820 825 830
 Leu Leu Ala Glu Ser Ser Asn Pro Ala Thr Leu Glu Gly Ser Ala Gly
 835 840 845
 Ser Leu Gln Asn Leu Ser Ala Ser Asn Trp Lys Phe Ala Ala Tyr Ile
 850 855 860
 Arg Gly Gly Arg Pro Lys Arg Lys Gly Leu Pro Ile Leu Val Glu Leu
 865 870 875 880
 Leu Arg Met Asp Asn Asp Arg Val Val Ser Ser Gly Ala Thr Ala Leu
 885 890 895
 Arg Asn Met Ala Leu Asp Val Arg Asn Lys Glu Leu Ile Gly Lys Tyr
 900 905 910
 Ala Met Arg Asp Leu Val Asn Arg Leu Pro Gly Gly Asn Gly Pro Ser
 915 920 925
 Val Leu Ser Asp Glu Thr Met Ala Ala Ile Cys Cys Ala Leu His Glu
 930 935 940
 Val Thr Ser Lys Asn Met Glu Asn Ala Lys Ala Leu Ala Asp Ser Gly
 945 950 955 960
 Gly Ile Glu Lys Leu Val Asn Ile Thr Lys Gly Arg Gly Asp Arg Ser
 965 970 975
 Ser Leu Lys Val Val Lys Ala Ala Ala Gln Val Leu Asn Thr Leu Trp
 980 985 990
 Gln Tyr Arg Asp Leu Arg Ser Ile Tyr Lys Lys Asp Gly Trp Asn Gln
 995 1000 1005
 Asn His Phe Ile Thr Pro Val Ser Thr Leu Glu Arg Asp Arg Phe
 1010 1015 1020
 Lys Ser His Pro Ser Leu Ser Thr Thr Asn Gln Gln Met Ser Pro
 1025 1030 1035
 Ile Ile Gln Ser Val Gly Ser Thr Ser Ser Ser Pro Ala Leu Leu
 1040 1045 1050

Protein Complexes associated with APP-processing
 Gly Ile Arg Asp Pro Arg Ser Glu Tyr Asp Arg Thr Gln Pro Pro
 1055 1060 1065

Met Gln Tyr Tyr Asn Ser Gln Gly Asp Ala Thr His Lys Gly Leu
 1070 1075 1080

Tyr Pro Gly Ser Ser Lys Pro Ser Pro Ile Tyr Ile Ser Ser Tyr
 1085 1090 1095

Ser Ser Pro Ala Arg Glu Gln Asn Arg Arg Leu Gln His Gln Gln
 1100 1105 1110

Leu Tyr Tyr Ser Gln Asp Asp Ser Asn Arg Lys Asn Phe Asp Ala
 1115 1120 1125

Tyr Arg Leu Tyr Leu Gln Ser Pro His Ser Tyr Glu Asp Pro Tyr
 1130 1135 1140

Phe Asp Asp Arg Val His Phe Pro Ala Ser Thr Asp Tyr Ser Thr
 1145 1150 1155

Gln Tyr Gly Leu Lys Ser Thr Thr Asn Tyr Val Asp Phe Tyr Ser
 1160 1165 1170

Thr Lys Arg Pro Ser Tyr Arg Ala Glu Gln Tyr Pro Gly Ser Pro
 1175 1180 1185

Asp Ser Trp Val Tyr Asp Gln Asp Ala Gln Gln Arg Asn Ser Phe
 1190 1195 1200

Phe Leu Thr Leu Phe Arg Leu Arg
 1205 1210

<210> 17

<211> 463

<212> PRT

<213> Homo sapiens

<400> 17

Met Thr Glu Leu Pro Ala Pro Leu Ser Tyr Phe Gln Asn Ala Gln Met
 1 5 10 15

Ser Glu Asp Asn His Leu Ser Asn Thr Asn Asp Asn Arg Glu Arg Gln
 20 25 30

Glu His Asn Asp Arg Arg Ser Leu Gly His Pro Glu Pro Leu Ser Asn
 35 40 45

Protein Complexes associated with APP-processing

Gly Arg Pro Gln Gly Asn Ser Arg Gln Val Val Glu Gln Asp Glu Glu
50 55 60

Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly Ala Lys His Val Ile Met
65 70 75 80

Leu Phe Val Pro Val Thr Leu Cys Met Val Val Val Val Ala Thr Ile
85 90 95

Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp Gly Gln Leu Ile Tyr Thr
100 105 110

Pro Phe Thr Glu Asp Thr Glu Thr Val Gly Gln Arg Ala Leu His Ser
115 120 125

Ile Leu Asn Ala Ala Ile Met Ile Ser Val Ile Val Val Met Thr Ile
130 135 140

Leu Leu Val Val Leu Tyr Lys Tyr Arg Cys Tyr Lys Val Ile His Ala
145 150 155 160

Trp Leu Ile Ile Ser Ser Leu Leu Leu Leu Phe Phe Phe Ser Phe Ile
165 170 175

Tyr Leu Gly Glu Val Phe Lys Thr Tyr Asn Val Ala Val Asp Tyr Ile
180 185 190

Thr Val Ala Leu Leu Ile Trp Asn Leu Gly Val Val Gly Met Ile Ser
195 200 205

Ile His Trp Lys Gly Pro Leu Arg Leu Gln Gln Ala Tyr Leu Ile Met
210 215 220

Ile Ser Ala Leu Met Ala Leu Val Phe Ile Lys Tyr Leu Pro Glu Trp
225 230 235 240

Thr Ala Trp Leu Ile Leu Ala Val Ile Ser Val Tyr Asp Leu Val Ala
245 250 255

Val Leu Cys Pro Lys Gly Pro Leu Arg Met Leu Val Glu Thr Ala Gln
260 265 270

Glu Arg Asn Glu Thr Leu Phe Pro Ala Leu Ile Tyr Ser Ser Thr Met
275 280 285

Val Trp Leu Val Asn Met Ala Glu Gly Asp Pro Glu Ala Gln Arg Arg
290 295 300

Val Ser Lys Asn Ser Lys Tyr Asn Ala Glu Ser Thr Glu Arg Glu Ser
305 310 315 320

Protein Complexes associated with APP-processing

Val Gln Pro Phe Met Asp Gln Leu Ala Phe His Gln Phe Tyr Ile
450 455 460

<210> 18

<211> 831

<212> PRT

<213> Homo sapiens

<400> 18

Met Glu Arg Pro Trp Gly Ala Ala Asp Gly Leu Ser Arg Trp Pro His
1 5 10 15

Gly Leu Gly Leu Leu Leu Leu Gln Leu Leu Pro Pro Ser Thr Leu
20 25 30

Ser Gln Asp Arg Leu Asp Ala Pro Pro Pro Pro Ala Ala Pro Leu Pro
35 40 45

Arg Trp Ser Gly Pro Ile Gly Val Ser Trp Gly Leu Arg Ala Ala Ala
50 55 60

Ala Gly Gly Ala Phe Pro Arg Gly Gly Arg Trp Arg Arg Ser Ala Pro
65 70 75 80

Protein Complexes associated with APP-processing

Gly Glu Asp Glu Glu Cys Gly Arg Val Arg Asp Phe Val Ala Lys Leu
85 90 95

Ala Asn Asn Thr His Gln His Val Phe Asp Asp Leu Arg Gly Ser Val
100 105 110

Ser Leu Ser Trp Val Gly Asp Ser Thr Gly Val Ile Leu Val Leu Thr
115 120 125

Thr Phe His Val Pro Leu Val Ile Met Thr Phe Gly Gln Ser Lys Leu
130 135 140

Tyr Arg Ser Glu Asp Tyr Gly Lys Asn Phe Lys Asp Ile Thr Asp Leu
145 150 155 160

Ile Asn Asn Thr Phe Ile Arg Thr Glu Phe Gly Met Ala Ile Gly Pro
165 170 175

Glu Asn Ser Gly Lys Val Val Leu Thr Ala Glu Val Ser Gly Gly Ser
180 185 190

Arg Gly Gly Arg Ile Phe Arg Ser Ser Asp Phe Ala Lys Asn Phe Val
195 200 205

Gln Thr Asp Leu Pro Phe His Pro Leu Thr Gln Met Met Tyr Ser Pro
210 215 220

Gln Asn Ser Asp Tyr Leu Leu Ala Leu Ser Thr Glu Asn Gly Leu Trp
225 230 235 240

Val Ser Lys Asn Phe Gly Gly Lys Trp Glu Glu Ile His Lys Ala Val
245 250 255

Cys Leu Ala Lys Trp Gly Ser Asp Asn Thr Ile Phe Phe Thr Thr Tyr
260 265 270

Ala Asn Gly Ser Cys Lys Ala Asp Leu Gly Ala Leu Glu Leu Trp Arg
275 280 285

Thr Ser Asp Leu Gly Lys Ser Phe Lys Thr Ile Gly Val Lys Ile Tyr
290 295 300

Ser Phe Gly Leu Gly Gly Arg Phe Leu Phe Ala Ser Val Met Ala Asp
305 310 315 320

Lys Asp Thr Thr Arg Arg Ile His Val Ser Thr Asp Gln Gly Asp Thr
325 330 335

Trp Ser Met Ala Gln Leu Pro Ser Val Gly Gln Glu Gln Phe Tyr Ser
340 345 350

Protein Complexes associated with APP-processing

Ile Leu Ala Ala Asn Asp Asp Met Val Phe Met His Val Asp Glu Pro
 355 360 365

Gly Asp Thr Gly Phe Gly Thr Ile Phe Thr Ser Asp Asp Arg Gly Ile
 370 375 380

Val Tyr Ser Lys Ser Leu Asp Arg His Leu Tyr Thr Thr Thr Gly Gly
 385 390 395 400

Glu Thr Asp Phe Thr Asn Val Thr Ser Leu Arg Gly Val Tyr Ile Thr
 405 410 415

Ser Val Leu Ser Glu Asp Asn Ser Ile Gln Thr Met Ile Thr Phe Asp
 420 425 430

Gln Gly Gly Arg Trp Thr His Leu Arg Lys Pro Glu Asn Ser Glu Cys
 435 440 445

Asp Ala Thr Ala Lys Asn Lys Asn Glu Cys Ser Leu His Ile His Ala
 450 455 460

Ser Tyr Ser Ile Ser Gln Lys Leu Asn Val Pro Met Ala Pro Leu Ser
 465 470 475 480

Glu Pro Asn Ala Val Gly Ile Val Ile Ala His Gly Ser Val Gly Asp
 485 490 495

Ala Ile Ser Val Met Val Pro Asp Val Tyr Ile Ser Asp Asp Gly Gly
 500 505 510

Tyr Ser Trp Thr Lys Met Leu Glu Gly Pro His Tyr Tyr Thr Ile Leu
 515 520 525

Asp Ser Gly Gly Ile Ile Val Ala Ile Glu His Ser Ser Arg Pro Ile
 530 535 540

Asn Val Ile Lys Phe Ser Thr Asp Glu Gly Gln Cys Trp Gln Thr Tyr
 545 550 555 560

Thr Phe Thr Arg Asp Pro Ile Tyr Phe Thr Gly Leu Ala Ser Glu Pro
 565 570 575

Gly Ala Arg Ser Met Asn Ile Ser Ile Trp Gly Phe Thr Glu Ser Phe
 580 585 590

Leu Thr Ser Gln Trp Val Ser Tyr Thr Ile Asp Phe Lys Asp Ile Leu
 595 600 605

Glu Arg Asn Cys Glu Glu Lys Asp Tyr Thr Ile Trp Leu Ala His Ser
 610 615 620

Protein Complexes associated with APP-processing
 Thr Asp Pro Glu Asp Tyr Glu Asp Gly Cys Ile Leu Gly Tyr Lys Glu
 625 630 635 640

Gln Phe Leu Arg Leu Arg Lys Ser Ser Met Cys Gln Asn Gly Arg Asp
 645 650 655

Tyr Val Val Thr Lys Gln Pro Ser Ile Cys Leu Cys Ser Leu Glu Asp
 660 665 670

Phe Leu Cys Asp Phe Gly Tyr Tyr Arg Pro Glu Asn Asp Ser Lys Cys
 675 680 685

Val Glu Gln Pro Glu Leu Lys Gly His Asp Leu Glu Phe Cys Leu Tyr
 690 695 700

Gly Arg Glu Glu His Leu Thr Thr Asn Gly Tyr Arg Lys Ile Pro Gly
 705 710 715 720

Asp Lys Cys Gln Gly Gly Val Asn Pro Val Arg Glu Val Lys Asp Leu
 725 730 735

Lys Lys Lys Cys Thr Ser Asn Phe Leu Ser Pro Glu Lys Gln Asn Ser
 740 745 750

Lys Ser Asn Ser Val Pro Ile Ile Leu Ala Ile Val Gly Leu Met Leu
 755 760 765

Val Thr Val Val Ala Gly Val Leu Ile Val Lys Lys Tyr Val Cys Gly
 770 775 780

Gly Arg Phe Leu Val His Arg Tyr Ser Val Leu Gln Gln His Ala Glu
 785 790 795 800

Ala Asn Gly Val Asp Gly Val Asp Ala Leu Asp Thr Ala Ser His Thr
 805 810 815

Asn Lys Ser Gly Tyr His Asp Asp Ser Asp Glu Asp Leu Leu Glu
 820 825 830

<210> 19

<211> 690

<212> PRT

<213> Homo sapiens

<400> 19

Met Gly Ala Val Ala Arg Ala His Gly Gly Leu Arg Val Ala Arg Ala
 1 5 10 15

Protein Complexes associated with APP-processing

Arg Glu Ser Val Ala Gly Gly Arg His Arg Gly Ala Gly Arg Pro Gly

20 25 30

Arg Phe Ala Arg Cys Leu Val Asp Ala Ser Asp Thr Ser Gln Gly Arg
275 280 285

Protein Complexes associated with APP-processing

Gly Pro Asp Asp Leu Gln Arg Leu Val Pro Leu Asp Ser Asn Arg
 290 295 300

Leu Glu Ala Gln Cys Ile Gly Ala Phe Tyr Leu Cys Ala Glu Ala Ala
 305 310 315 320

Ile Lys Ser Leu Gln Gly Lys Thr Lys Val Phe Ser Asp Ile Gly Ala
 325 330 335

Ile Gln Ser Leu Lys Arg Leu Val Ser Tyr Ser Thr Asn Gly Thr Lys
 340 345 350

Ser Ala Leu Ala Lys Arg Ala Leu Arg Leu Leu Gly Glu Glu Val Pro
 355 360 365

Arg Pro Ile Leu Pro Ser Val Pro Ser Trp Lys Glu Ala Glu Val Gln
 370 375 380

Thr Trp Leu Gln Gln Ile Gly Phe Ser Lys Tyr Cys Glu Ser Phe Arg
 385 390 395 400

Glu Gln Gln Val Asp Gly Asp Leu Leu Leu Arg Leu Thr Glu Glu Glu
 405 410 415

Leu Gln Thr Asp Leu Gly Met Lys Ser Gly Ile Thr Arg Lys Arg Phe
 420 425 430

Phe Arg Glu Leu Thr Glu Leu Lys Thr Phe Ala Asn Tyr Ser Thr Cys
 435 440 445

Asp Arg Ser Asn Leu Ala Asp Trp Leu Gly Ser Leu Asp Pro Arg Phe
 450 455 460

Arg Gln Tyr Thr Tyr Gly Leu Val Ser Cys Gly Leu Asp Arg Ser Leu
 465 470 475 480

Leu His Arg Val Ser Glu Gln Gln Leu Leu Glu Asp Cys Gly Ile His
 485 490 495

Leu Gly Val His Arg Ala Arg Ile Leu Thr Ala Ala Arg Glu Met Leu
 500 505 510

His Ser Pro Leu Pro Cys Thr Gly Gly Lys Pro Ser Gly Asp Thr Pro
 515 520 525

Asp Val Phe Ile Ser Tyr Arg Arg Asn Ser Gly Ser Gln Leu Ala Ser
 530 535 540

Leu Leu Lys Val His Leu Gln Leu His Gly Phe Ser Val Phe Ile Asp
 545 550 555 560

Protein complexes associated with APP processing

Val	Glu	Lys	Leu	Glu	Ala	Gly	Lys	Phe	Glu	Asp	Lys	Leu	Ile	Gln	Ser
				565					570					575	

Asp Lys Cys Met Gln Asp His Asp Cys Lys Asp Trp Val His Lys Glu
595 600 605

Gly Phe Glu Trp Pro Glu Pro Gln Val Leu Pro Glu Asp Met Gln Ala
625 630 635 640

Thr Ile Glu Lys Ile Ile Arg Phe Leu Gln Gly Arg Ser Ser Arg Asp
660 665 670

Ser Ser Ala Gly Ser Asp Thr Ser Leu Glu Gly Ala Ala Pro Met Gly
675 680 685

Pro Thr
690

<210> 20

<211> 589

<212> PRT

<213> Homo sapiens

<400> 20

Met Ala Glu Ser Gly Glu Ser Gly Gly Pro Pro Gly Ser Gln Asp Ser
1 5 10 15

Ala Ala Gly Ala Glu Gly Ala Gly Ala Pro Ala Ala Ala Ala Ser Ala
20 25 30

Glu Pro Lys Ile Met Lys Val Thr Val Lys Thr Pro Lys Glu Lys Glu
35 40 45

Glu Phe Ala Val Pro Glu Asn Ser Ser Val Gln Gln Phe Lys Glu Glu
50 55 60

Ile Ser Lys Arg Phe Lys Ser His Thr Asp Gln Leu Val Leu Ile Phe.
65 70 75 80

Protein Complexes associated with APP-processing

Ala Gly Lys Ile Leu Lys Asp Gln Asp Thr Leu Ser Gln His Gly Ile
85 90 95

His Asp Gly Leu Thr Val His Leu Val Ile Lys Thr Gln Asn Arg Pro
100 105 110

Gln Asp His Ser Ala Gln Gln Thr Asn Thr Ala Gly Ser Asn Val Thr
115 120 125

Thr Ser Ser Thr Pro Asn Ser Asn Ser Thr Ser Gly Ser Ala Thr Ser
130 135 140

Asn Pro Phe Gly Leu Gly Gly Leu Gly Gly Leu Ala Gly Leu Ser Ser
145 150 155 160

Leu Gly Leu Asn Thr Thr Asn Phe Ser Glu Leu Gln Ser Gln Met Gln
165 170 175

Arg Gln Leu Leu Ser Asn Pro Glu Met Met Val Gln Ile Met Glu Asn
180 185 190

Pro Phe Val Gln Ser Met Leu Ser Asn Pro Asp Leu Met Arg Gln Leu
195 200 205

Ile Met Ala Asn Pro Gln Met Gln Gln Leu Ile Gln Arg Asn Pro Glu
210 215 220

Ile Ser His Met Leu Asn Asn Pro Asp Ile Met Arg Gln Thr Leu Glu
225 230 235 240

Leu Ala Arg Asn Pro Ala Met Met Gln Glu Met Met Arg Asn Gln Asp
245 250 255

Arg Ala Leu Ser Asn Leu Glu Ser Ile Pro Gly Gly Tyr Asn Ala Leu
260 265 270

Arg Arg Met Tyr Thr Asp Ile Gln Glu Pro Met Leu Ser Ala Ala Gln
275 280 285

Glu Gln Phe Gly Gly Asn Pro Phe Ala Ser Leu Val Ser Asn Thr Ser
290 295 300

Ser Gly Glu Gly Ser Gln Pro Ser Arg Thr Glu Asn Arg Asp Pro Leu
305 310 315 320

Pro Asn Pro Trp Ala Pro Gln Thr Ser Gln Ser Ser Ser Ala Ser Ser
325 330 335

Gly Thr Ala Ser Thr Val Gly Gly Thr Thr Gly Ser Thr Ala Ser Gly
340 345 350

Protein Complexes associated with APP-processing

Thr Ser Gly Gln Ser Thr Thr Ala Pro Asn Leu Val Pro Gly Val Gly
 355 360 365

Ala Ser Met Phe Asn Thr Pro Gly Met Gln Ser Leu Leu Gln Gln Ile
 370 375 380

Thr Glu Asn Pro Gln Leu Met Gln Asn Met Leu Ser Ala Pro Tyr Met
 385 390 395 400

Arg Ser Met Met Gln Ser Leu Ser Gln Asn Pro Asp Leu Ala Ala Gln
 405 410 415

Met Met Leu Asn Asn Pro Leu Phe Ala Gly Asn Pro Gln Leu Gln Glu
 420 425 430

Gln Met Arg Gln Gln Leu Pro Thr Phe Leu Gln Gln Met Gln Asn Pro
 435 440 445

Asp Thr Leu Ser Ala Met Ser Asn Pro Arg Ala Met Gln Ala Leu Leu
 450 455 460

Gln Ile Gln Gln Gly Leu Gln Thr Leu Ala Thr Glu Ala Pro Gly Leu
 465 470 475 480

Ile Pro Gly Phe Thr Pro Gly Leu Gly Ala Leu Gly Ser Thr Gly Gly
 485 490 495

Ser Ser Gly Thr Asn Gly Ser Asn Ala Thr Pro Ser Glu Asn Thr Ser
 500 505 510

Pro Thr Ala Gly Thr Thr Glu Pro Gly His Gln Gln Phe Ile Gln Gln
 515 520 525

Met Leu Gln Ala Leu Ala Gly Val Asn Pro Gln Leu Gln Asn Pro Glu
 530 535 540

Val Arg Phe Gln Gln Gln Leu Glu Gln Leu Ser Ala Met Gly Phe Leu
 545 550 555 560

Asn Arg Glu Ala Asn Leu Gln Ala Leu Ile Ala Thr Gly Gly Asp Ile
 565 570 575

Asn Ala Ala Ile Glu Arg Leu Leu Gly Ser Gln Pro Ser
 580 585

<210> 21

<211> 255

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 21

Met Asp Asp Arg Glu Asp Leu Val Tyr Gln Ala Lys Leu Ala Glu Gln
 1 5 10 15

Ala Glu Arg Tyr Asp Glu Met Val Glu Ser Met Lys Lys Val Ala Gly
 20 25 30

Met Asp Val Glu Leu Thr Val Glu Glu Arg Asn Leu Leu Ser Val Ala
 35 40 45

Tyr Lys Asn Val Ile Gly Ala Arg Arg Ala Ser Trp Arg Ile Ile Ser
 50 55 60

Ser Ile Glu Gln Lys Glu Glu Asn Lys Gly Gly Glu Asp Lys Leu Lys
 65 70 75 80

Met Ile Arg Glu Tyr Arg Gln Met Val Glu Thr Glu Leu Lys Leu Ile
 85 90 95

Cys Cys Asp Ile Leu Asp Val Leu Asp Lys His Leu Ile Pro Ala Ala
 100 105 110

Asn Thr Gly Glu Ser Lys Val Phe Tyr Tyr Lys Met Lys Gly Asp Tyr
 115 120 125

His Arg Tyr Leu Ala Glu Phe Ala Thr Gly Asn Asp Arg Lys Glu Ala
 130 135 140

Ala Glu Asn Ser Leu Val Ala Tyr Lys Ala Ala Ser Asp Ile Ala Met
 145 150 155 160

Thr Glu Leu Pro Pro Thr His Pro Ile Arg Leu Gly Leu Ala Leu Asn
 165 170 175

Phe Ser Val Phe Tyr Tyr Glu Ile Leu Asn Ser Pro Asp Arg Ala Cys
 180 185 190

Arg Leu Ala Lys Ala Ala Phe Asp Asp Ala Ile Ala Glu Leu Asp Thr
 195 200 205

Leu Ser Glu Glu Ser Tyr Lys Asp Ser Thr Leu Ile Met Gln Leu Leu
 210 215 220

Arg Asp Asn Leu Thr Leu Trp Thr Ser Asp Met Gln Gly Asp Gly Glu
 225 230 235 240

Glu Gln Asn Lys Glu Ala Leu Gln Asp Val Glu Asp Glu Asn Gln
 245 250 255

Protein Complexes associated with APP-processing

<210> 22

<211> 245

<212> PRT

<213> Homo sapiens

<400> 22

Thr Met Asp Lys Ser Glu Leu Val Gln Lys Ala Lys Leu Ala Glu Gln
 1 5 10 15

Ala Glu Arg Tyr Asp Asp Met Ala Ala Ala Met Lys Ala Val Thr Glu
 20 25 30

Gln Gly His Glu Leu Ser Asn Glu Glu Arg Asn Leu Leu Ser Val Ala
 35 40 45

Tyr Lys Asn Val Val Gly Ala Arg Arg Ser Ser Trp Arg Val Ile Ser
 50 55 60

Ser Ile Glu Gln Lys Thr Glu Arg Asn Glu Lys Lys Gln Gln Met Gly
 65 70 75 80

Lys Glu Tyr Arg Glu Lys Ile Glu Ala Glu Leu Gln Asp Ile Cys Asn
 85 90 95

Asp Val Leu Glu Leu Leu Asp Lys Tyr Leu Ile Pro Asn Ala Thr Gln
 100 105 110

Pro Glu Ser Lys Val Phe Tyr Leu Lys Met Lys Gly Asp Tyr Phe Arg
 115 120 125

Tyr Leu Ser Glu Val Ala Ser Gly Asp Asn Lys Gln Thr Thr Val Ser
 130 135 140

Asn Ser Gln Gln Ala Tyr Gln Glu Ala Phe Glu Ile Ser Lys Lys Glu
 145 150 155 160

Met Gln Pro Thr His Pro Ile Arg Leu Gly Leu Ala Leu Asn Phe Ser
 165 170 175

Val Phe Tyr Tyr Glu Ile Leu Asn Ser Pro Glu Lys Ala Cys Ser Leu
 180 185 190

Ala Lys Thr Ala Phe Asp Glu Ala Ile Ala Glu Leu Asp Thr Leu Asn
 195 200 205

Glu Glu Ser Tyr Lys Asp Ser Thr Leu Ile Met Gln Leu Leu Arg Asp
 210 215 220

Protein Complexes associated with APP-processing
 Asn Leu Thr Leu Trp Thr Ser Glu Asn Gln Gly Asp Glu Gly Asp Ala
 225 230 235 240

Gly Glu Gly Glu Asn
 245

<210> 23

<211> 245

<212> PRT

<213> Homo sapiens

<400> 23

Gly Asp Arg Glu Gln Leu Leu Gln Arg Ala Arg Leu Ala Glu Gln Ala
 1 5 10 15

Glu Arg Tyr Asp Asp Met Ala Ser Ala Met Lys Ala Val Thr Glu Leu
 20 25 30

Asn Glu Pro Leu Ser Asn Glu Asp Arg Asn Leu Leu Ser Val Ala Tyr
 35 40 45

Lys Asn Val Val Gly Ala Arg Arg Ser Ser Trp Arg Val Ile Ser Ser
 50 55 60

Ile Glu Gln Lys Thr Met Ala Asp Gly Asn Glu Lys Lys Leu Glu Lys
 65 70 75 80

Val Lys Ala Tyr Arg Glu Lys Ile Glu Lys Glu Leu Glu Thr Val Cys
 85 90 95

Asn Asp Val Leu Ser Leu Leu Asp Lys Phe Leu Ile Lys Asn Cys Asn
 100 105 110

Asp Phe Gln Tyr Glu Ser Lys Val Phe Tyr Leu Lys Met Lys Gly Asp
 115 120 125

Tyr Tyr Arg Tyr Leu Ala Glu Val Ala Ser Gly Glu Lys Lys Asn Ser
 130 135 140

Val Val Glu Ala Ser Glu Ala Ala Tyr Lys Glu Ala Phe Glu Ile Ser
 145 150 155 160

Lys Glu Gln Met Gln Pro Thr His Pro Ile Arg Leu Gly Leu Ala Leu
 165 170 175

Asn Phe Ser Val Phe Tyr Tyr Glu Ile Gln Asn Ala Pro Glu Gln Ala
 180 185 190

Protein Complexes associated with APP-processing

Cys Leu Leu Ala Lys Gln Ala Phe Asp Asp Ala Ile Ala Glu Leu Asp
 195 200 205

Thr Leu Asn Glu Asp Ser Tyr Lys Asp Ser Thr Leu Ile Met Gln Leu
 210 215 220

Leu Arg Asp Asn Leu Thr Leu Trp Thr Ser Asp Gln Gln Asp Glu Glu
 225 230 235 240

Ala Gly Glu Gly Asn
 245

<210> 24

<211> 246

<212> PRT

<213> Homo sapiens

<400> 24

Val Asp Arg Glu Gln Leu Val Gln Lys Ala Arg Leu Ala Glu Gln Ala
 1 5 10 15

Glu Arg Tyr Asp Asp Met Ala Ala Ala Met Lys Asn Val Thr Glu Leu
 20 25 30

Asn Glu Pro Leu Ser Asn Glu Glu Arg Asn Leu Leu Ser Val Ala Tyr
 35 40 45

Lys Asn Val Val Gly Ala Arg Arg Ser Ser Trp Arg Val Ile Ser Ser
 50 55 60

Ile Glu Gln Lys Thr Ser Ala Asp Gly Asn Glu Lys Lys Ile Glu Met
 65 70 75 80

Val Arg Ala Tyr Arg Glu Lys Ile Glu Lys Glu Leu Glu Ala Val Cys
 85 90 95

Gln Asp Val Leu Ser Leu Leu Asp Asn Tyr Leu Ile Lys Asn Cys Ser
 100 105 110

Glu Thr Gln Tyr Glu Ser Lys Val Phe Tyr Leu Lys Met Lys Gly Asp
 115 120 125

Tyr Tyr Arg Tyr Leu Ala Glu Val Ala Thr Gly Glu Lys Arg Ala Thr
 130 135 140

Val Val Glu Ser Ser Glu Lys Ala Tyr Ser Glu Ala His Glu Ile Ser
 145 150 155 160

Protein Complexes associated with APP-processing
 Lys Glu His Met Gln Pro Thr His Pro Ile Arg Leu Gly Leu Ala Leu
 165 170 175

Asn Tyr Ser Val Phe Tyr Tyr Glu Ile Gln Asn Ala Pro Glu Gln Ala
 180 185 190

Cys His Leu Ala Lys Thr Ala Phe Asp Asp Ala Ile Ala Glu Leu Asp
 195 200 205

Thr Leu Asn Glu Asp Ser Tyr Lys Asp Ser Thr Leu Ile Met Gln Leu
 210 215 220

Leu Arg Asp Asn Leu Thr Leu Trp Thr Ser Asp Gln Gln Asp Asp Asp
 225 230 235 240

Gly Gly Glu Gly Asn Asn
 245

<210> 25

<211> 245

<212> PRT

<213> Homo sapiens

<400> 25

Met Glu Lys Thr Glu Leu Ile Gln Lys Ala Lys Leu Ala Glu Gln Ala
 1 5 10 15

Glu Arg Tyr Asp Asp Met Ala Thr Cys Met Lys Ala Val Thr Glu Gln
 20 25 30

Gly Ala Glu Leu Ser Asn Glu Glu Arg Asn Leu Leu Ser Val Ala Tyr
 35 40 45

Lys Asn Val Val Gly Gly Arg Arg Ser Ala Trp Arg Val Ile Ser Ser
 50 55 60

Ile Glu Gln Lys Thr Asp Thr Ser Asp Lys Lys Leu Gln Leu Ile Lys
 65 70 75 80

Asp Tyr Arg Glu Lys Val Glu Ser Glu Leu Arg Ser Ile Cys Thr Thr
 85 90 95

Val Leu Glu Leu Leu Asp Lys Tyr Leu Ile Ala Asn Ala Thr Asn Pro
 100 105 110

Glu Ser Lys Val Phe Tyr Leu Lys Met Lys Gly Asp Tyr Phe Arg Tyr
 115 120 125

Protein Complexes associated with APP-processing
 Leu Ala Glu Val Ala Cys Gly Asp Asp Arg Lys Gln Thr Ile Asp Asn
 130 135 140

Ser Gln Gly Ala Tyr Gln Glu Ala Phe Asp Ile Ser Lys Lys Glu Met
 145 150 155 160

Gln Pro Thr His Pro Ile Arg Leu Gly Leu Ala Leu Asn Phe Ser Val
 165 170 175

Phe Tyr Tyr Glu Ile Leu Asn Asn Pro Glu Leu Ala Cys Thr Leu Ala
 180 185 190

Lys Thr Ala Phe Asp Glu Ala Ile Ala Glu Leu Asp Thr Leu Asn Glu
 195 200 205

Asp Ser Tyr Lys Asp Ser Thr Leu Ile Met Gln Leu Leu Arg Asp Asn
 210 215 220

Leu Thr Leu Trp Thr Ser Asp Ser Ala Gly Glu Glu Cys Asp Ala Ala
 225 230 235 240

Glu Gly Ala Glu Asn
 245

<210> 26

<211> 245

<212> PRT

<213> Homo sapiens

<400> 26

Met Asp Lys Asn Glu Leu Val Gln Lys Ala Lys Leu Ala Glu Gln Ala
 1 5 10 15

Glu Arg Tyr Asp Asp Met Ala Ala Cys Met Lys Ser Val Thr Glu Gln
 20 25 30

Gly Ala Glu Leu Ser Asn Glu Glu Arg Asn Leu Leu Ser Val Ala Tyr
 35 40 45

Lys Asn Val Val Gly Ala Arg Arg Ser Ser Trp Arg Val Val Ser Ser
 50 55 60

Ile Glu Gln Lys Thr Glu Gly Ala Glu Lys Lys Gln Gln Met Ala Arg
 65 70 75 80

Glu Tyr Arg Glu Lys Ile Glu Thr Glu Leu Arg Asp Ile Cys Asn Asp
 85 90 95

Protein Complexes associated with APP-processing
 Val Leu Ser Leu Leu Glu Lys Phe Leu Ile Pro Asn Ala Ser Gln Ala
 100 105 110

Glu Ser Lys Val Phe Tyr Leu Lys Met Lys Gly Asp Tyr Tyr Arg Tyr
 115 120 125

Leu Ala Glu Val Ala Ala Gly Asp Asp Lys Lys Gly Ile Val Asp Gln
 130 135 140

Ser Gln Gln Ala Tyr Gln Glu Ala Phe Glu Ile Ser Lys Lys Glu Met
 145 150 155 160

Gln Pro Thr His Pro Ile Arg Leu Gly Leu Ala Leu Asn Phe Ser Val
 165 170 175

Phe Tyr Tyr Glu Ile Leu Asn Ser Pro Glu Lys Ala Cys Ser Leu Ala
 180 185 190

Lys Thr Ala Phe Asp Glu Ala Ile Ala Glu Leu Asp Thr Leu Ser Glu
 195 200 205

Glu Ser Tyr Lys Asp Ser Thr Leu Ile Met Gln Leu Leu Arg Asp Asn
 210 215 220

Leu Thr Leu Trp Thr Ser Asp Thr Gln Gly Asp Glu Ala Glu Ala Gly
 225 230 235 240

Glu Gly Gly Glu Asn
 245

<210> 27

<211> 650

<212> PRT

<213> Homo sapiens

<400> 27

Met Gly Pro Ala Ser Pro Ala Ala Arg Gly Leu Ser Arg Arg Pro Gly
 1 5 10 15

Gln Pro Pro Leu Pro Leu Leu Leu Pro Leu Leu Leu Leu Leu Arg
 20 25 30

Ala Gln Pro Ala Ile Gly Ser Leu Ala Gly Gly Ser Pro Gly Ala Pro
 35 40 45

Glu Ala Pro Gly Ser Ala Gln Val Ala Gly Leu Cys Gly Arg Leu Thr
 50 55 60

Protein Complexes associated with APP-processing

Leu His Arg Asp Leu Arg Thr Gly Arg Trp Glu Pro Asp Pro Gln Arg
 65 70 75 80

Ser Arg Arg Cys Leu Arg Asp Pro Gln Arg Val Leu Glu Tyr Cys Arg
 85 90 95

Gln Met Tyr Pro Glu Leu Gln Ile Ala Arg Val Glu Gln Ala Thr Gln
 100 105 110

Ala Ile Pro Met Glu Arg Trp Cys Gly Gly Ser Arg Ser Gly Ser Cys
 115 120 125

Ala His Pro His His Gln Val Val Pro Phe Arg Cys Leu Pro Gly Glu
 130 135 140

Phe Val Ser Glu Ala Leu Leu Val Pro Glu Gly Cys Arg Phe Leu His
 145 150 155 160

Gln Glu Arg Met Asp Gln Cys Glu Ser Ser Thr Arg Arg His Gln Glu
 165 170 175

Ala Gln Glu Ala Cys Ser Ser Gln Gly Leu Ile Leu His Gly Ser Gly
 180 185 190

Met Leu Leu Pro Cys Gly Ser Asp Arg Phe Arg Gly Val Glu Tyr Val
 195 200 205

Cys Cys Pro Pro Pro Gly Thr Pro Asp Pro Ser Gly Thr Ala Val Gly
 210 215 220

Asp Pro Ser Thr Arg Ser Trp Pro Pro Gly Ser Arg Val Glu Gly Ala
 225 230 235 240

Glu Asp Glu Glu Glu Glu Glu Ser Phe Pro Gln Pro Val Asp Asp Tyr
 245 250 255

Phe Val Glu Pro Pro Gln Ala Glu Glu Glu Glu Thr Val Pro Pro
 260 265 270

Pro Ser Ser His Thr Leu Ala Val Val Gly Lys Val Thr Pro Thr Pro
 275 280 285

Arg Pro Thr Asp Gly Val Asp Ile Tyr Phe Gly Met Pro Gly Glu Ile
 290 295 300

Ser Glu His Glu Gly Phe Leu Arg Ala Lys Met Asp Leu Glu Glu Arg
 305 310 315 320

Arg Met Arg Gln Ile Asn Glu Val Met Arg Glu Trp Ala Met Ala Asp
 325 330 335

Protein Complexes associated with APP-processing

Asn Gln Ser Lys Asn Leu Pro Lys Ala Asp Arg Gln Ala Leu Asn Glu
 340 345 350

His Phe Gln Ser Ile Leu Gln Thr Leu Glu Glu Gln Val Ser Gly Glu
 355 360 365

Arg Gln Arg Leu Val Glu Thr His Ala Thr Arg Val Ile Ala Leu Ile
 370 375 380

Asn Asp Gln Arg Arg Ala Ala Leu Glu Gly Phe Leu Ala Ala Leu Gln
 385 390 395 400

Ala Asp Pro Pro Gln Ala Glu Arg Val Leu Leu Ala Leu Arg Arg Tyr
 405 410 415

Leu Arg Ala Glu Gln Lys Glu Gln Arg His Thr Leu Arg His Tyr Gln
 420 425 430

His Val Ala Ala Val Asp Pro Glu Lys Ala Gln Gln Met Arg Phe Gln
 435 440 445

Val His Thr His Leu Gln Val Ile Glu Glu Arg Val Asn Gln Ser Leu
 450 455 460

Gly Leu Leu Asp Gln Asn Pro His Leu Ala Gln Glu Leu Arg Pro Gln
 465 470 475 480

Ile Gln Glu Leu Leu His Ser Glu His Leu Gly Pro Ser Glu Leu Glu
 485 490 495

Ala Pro Ala Pro Gly Gly Ser Ser Glu Asp Lys Gly Gly Leu Gln Pro
 500 505 510

Pro Asp Ser Lys Asp Asp Thr Pro Met Thr Leu Pro Lys Gly Ser Thr
 515 520 525

Glu Gln Asp Ala Ala Ser Pro Glu Lys Glu Lys Met Asn Pro Leu Glu
 530 535 540

Gln Tyr Glu Arg Lys Val Asn Ala Ser Val Pro Arg Gly Phe Pro Phe
 545 550 555 560

His Ser Ser Glu Ile Gln Arg Asp Glu Leu Ala Pro Ala Gly Thr Gly
 565 570 575

Val Ser Arg Glu Ala Val Ser Gly Leu Leu Ile Met Gly Ala Gly Gly
 580 585 590

Gly Ser Leu Ile Val Leu Ser Met Leu Leu Leu Arg Arg Lys Lys Pro
 595 600 605

Protein Complexes associated with APP-processing
 Tyr Gly Ala Ile Ser His Gly Val Val Glu Val Asp Pro Met Leu Thr
 610 615 620

Leu Glu Glu Gln Gln Leu Arg Glu Leu Gln Arg His Gly Tyr Glu Asn
 625 630 635 640

Pro Thr Tyr Arg Phe Leu Glu Glu Arg Pro
 645 650

<210> 28

<211> 763

<212> PRT

<213> Homo sapiens

<400> 28

Met Ala Ala Thr Gly Thr Ala Ala Ala Ala Thr Gly Arg Leu Leu
 1 5 10 15

Leu Leu Leu Leu Val Gly Leu Thr Ala Pro Ala Leu Ala Leu Ala Gly
 20 25 30

Tyr Ile Glu Ala Leu Ala Ala Asn Ala Gly Thr Gly Phe Ala Val Ala
 35 40 45

Glu Pro Gln Ile Ala Met Phe Cys Gly Lys Leu Asn Met His Val Asn
 50 55 60

Ile Gln Thr Gly Lys Trp Glu Pro Asp Pro Thr Gly Thr Lys Ser Cys
 65 70 75 80

Phe Glu Thr Lys Glu Glu Val Leu Gln Tyr Cys Gln Glu Met Tyr Pro
 85 90 95

Glu Leu Gln Ile Thr Asn Val Met Glu Ala Asn Gln Arg Val Ser Ile
 100 105 110

Asp Asn Trp Cys Arg Arg Asp Lys Lys Gln Cys Lys Ser Arg Phe Val
 115 120 125

Thr Pro Phe Lys Cys Leu Val Gly Glu Phe Val Ser Asp Val Leu Leu
 130 135 140

Val Pro Glu Lys Cys Gln Phe Phe His Lys Glu Arg Met Glu Val Cys
 145 150 155 160

Glu Asn His Gln His Trp His Thr Val Val Lys Glu Ala Cys Leu Thr
 165 170 175

Protein Complexes associated with APP-processing

Gln	Gly	Met	Thr	Leu	Tyr	Ser	Tyr	Gly	Met	Leu	Leu	Pro	Cys	Gly	Val
			180					185					190		

His Phe Gln Ala Met Val Lys Ala Leu Glu Lys Glu Ala Ala Ser Glu
435 440 445

Protein Complexes associated with APP-processing

Lys Gln Gln Leu Val Glu Thr His Leu Ala Arg Val Glu Ala Met Leu
450 455 460

Asn Asp Arg Arg Arg Met Ala Leu Glu Asn Tyr Leu Ala Ala Leu Gln
465 470 475 480

Ser Asp Pro Pro Arg Pro His Arg Ile Leu Gln Ala Leu Arg Arg Tyr
485 490 495

Val Arg Ala Glu Asn Lys Asp Arg Leu His Thr Ile Arg His Tyr Gln
500 505 510

His Val Leu Ala Val Asp Pro Glu Lys Ala Ala Gln Met Lys Ser Gln
515 520 525

Val Met Thr His Leu His Val Ile Glu Glu Arg Arg Asn Gln Ser Leu
530 535 540

Ser Leu Leu Tyr Lys Val Pro Tyr Val Ala Gln Glu Ile Gln Glu Glu
545 550 555 560

Ile Asp Glu Leu Leu Gln Glu Gln Arg Ala Asp Met Asp Gln Phe Thr
565 570 575

Ala Ser Ile Ser Glu Thr Pro Val Asp Val Arg Val Ser Ser Glu Glu
580 585 590

Ser Glu Glu Ile Pro Pro Phe His Pro Phe His Pro Phe Pro Ala Leu
595 600 605

Pro Glu Asn Glu Asp Thr Gln Pro Glu Leu Tyr His Pro Met Lys Lys
610 615 620

Gly Ser Gly Val Gly Glu Gln Asp Gly Gly Leu Ile Gly Ala Glu Glu
625 630 635 640

Lys Val Ile Asn Ser Lys Asn Lys Val Asp Glu Asn Met Val Ile Asp
645 650 655

Glu Thr Leu Asp Val Lys Glu Met Ile Phe Asn Ala Glu Arg Val Gly
660 665 670

Gly Leu Glu Glu Glu Arg Glu Ser Val Gly Pro Leu Arg Glu Asp Phe
675 680 685

Ser Leu Ser Ser Ser Ala Leu Ile Gly Leu Leu Val Ile Ala Val Ala
690 695 700

Ile Ala Thr Val Ile Val Ile Ser Leu Val Met Leu Arg Lys Arg Gln
705 710 715 720

Protein Complexes associated with APP-processing
Tyr Gly Thr Ile Ser His Gly Ile Val Glu Val Asp Pro Met Leu Thr
725 730 735

Pro Thr Tyr Lys Tyr Leu Glu Gln Met Gln Ile
755 760

<213> Homo sapiens

Met Leu Pro Gly Leu Ala Leu Leu Leu Leu Ala Ala Trp Thr Ala Arg
1 5 10 15

Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro
20 25 30

Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
145 150 155 160

Lys Ser Thr Asn **Leu** His Asp Tyr Gly **Met** Leu Leu Pro Cys **Gly** Ile
165 170 175

Protein Complexes associated with APP-processing

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
275 280 285

Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile
290 295 300

Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe
305 310 315 320

Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr
325 330 335

Cys Met Ala Val Cys Gly Ser Ala Met Ser Gln Ser Leu Leu Lys Thr
340 345 350

Thr Gln Glu Pro Leu Ala Arg Asp Pro Val Lys Leu Pro Thr Thr Ala
355 360 365

Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp
370 375 380

Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala
385 390 395 400

Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala
405 410 415

Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile
420 425 430

Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn
435 440 445

Protein Complexes associated with APP-processing

Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met
 450 455 460

Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu
 465 470 475 480

Gln Ala Val Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys
 485 490 495

Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe
 500 505 510

Glu His Val Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser
 515 520 525

Gln Val Met Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser
 530 535 540

Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp
 545 550 555 560

Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val
 565 570 575

Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala
 580 585 590

Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro
 595 600 605

Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe
 610 615 620

Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val
 625 630 635 640

Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser
 645 650 655

Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp
 660 665 670

Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu
 675 680 685

Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly
 690 695 700

Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu
 705 710 715 720

Protein Complexes associated with APP-processing

Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys Phe Phe Glu Gln Met
755 760 765

<213> Homo sapiens

Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln
1 5 10 15

Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile
20 25 30

Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile
35 40 45

Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile His His Gly
50 55 60

Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser
65 70 75 80

Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys Phe Phe Glu
85 90 95

Gln Met Gln Asn
100

<213> Homo sapiens

<400> 31

Protein Complexes associated with APP-processing

Met Ala Leu Leu Ala Met His Ser Trp Arg Trp Ala Ala Ala Ala
 1 5 10 15
 Ala Phe Glu Lys Arg Arg His Ser Ala Ile Leu Ile Arg Pro Leu Val
 20 25 30
 Ser Val Ser Gly Ser Gly Pro Gln Trp Arg Pro His Gln Leu Gly Ala
 35 40 45
 Leu Gly Thr Ala Arg Ala Tyr Gln Ile Pro Glu Ser Leu Lys Ser Ile
 50 55 60
 Thr Trp Gln Arg Leu Gly Lys Gly Asn Ser Gly Gln Phe Leu Asp Ala
 65 70 75 80
 Ala Lys Ala Leu Gln Val Trp Pro Leu Ile Glu Lys Arg Thr Cys Trp
 85 90 95
 His Gly His Ala Gly Gly Gly Leu His Thr Asp Pro Lys Glu Gly Leu
 100 105 110
 Lys Asp Val Asp Thr Arg Lys Ile Ile Lys Ala Met Leu Ser Tyr Val
 115 120 125
 Trp Pro Lys Asp Arg Pro Asp Leu Arg Ala Arg Val Ala Ile Ser Leu
 130 135 140
 Gly Phe Leu Gly Gly Ala Lys Ala Met Asn Ile Val Val Pro Phe Met
 145 150 155 160
 Phe Lys Tyr Ala Val Asp Ser Leu Asn Gln Met Ser Gly Asn Met Leu
 165 170 175
 Asn Leu Ser Asp Ala Pro Asn Thr Val Ala Thr Met Ala Thr Ala Val
 180 185 190
 Leu Ile Gly Tyr Gly Val Ser Arg Ala Gly Ala Ala Phe Phe Asn Glu
 195 200 205
 Val Arg Asn Ala Val Phe Gly Lys Val Ala Gln Asn Ser Ile Arg Arg
 210 215 220
 Ile Ala Lys Asn Val Phe Leu His Leu His Asn Leu Asp Leu Gly Phe
 225 230 235 240
 His Leu Ser Arg Gln Thr Gly Ala Leu Ser Lys Ala Ile Asp Arg Gly
 245 250 255
 Thr Arg Gly Ile Ser Phe Val Leu Ser Ala Leu Val Phe Asn Leu Leu
 260 265 270

Protein Complexes associated with APP-processing
 Pro Ile Met Phe Glu Val Met Leu Val Ser Gly Val Leu Tyr Tyr Lys
 275 280 285

Cys Gly Ala Gln Phe Ala Leu Val Thr Leu Gly Thr Leu Gly Thr Tyr
 290 295 300

Thr Ala Phe Thr Val Ala Val Thr Arg Trp Arg Thr Arg Phe Arg Ile
 305 310 315 320

Glu Met Asn Lys Ala Asp Asn Asp Ala Gly Asn Ala Ala Ile Asp Ser
 325 330 335

Leu Leu Asn Tyr Glu Thr Val Lys Tyr Phe Asn Asn Glu Arg Tyr Glu
 340 345 350

Ala Gln Arg Tyr Asp Gly Phe Leu Lys Thr Tyr Glu Thr Ala Ser Leu
 355 360 365

Lys Ser Thr Ser Thr Leu Ala Met Leu Asn Phe Gly Gln Ser Ala Ile
 370 375 380

Phe Ser Val Gly Leu Thr Ala Ile Met Val Leu Ala Ser Gln Gly Ile
 385 390 395 400

Val Ala Gly Thr Leu Thr Val Gly Asp Leu Val Met Val Asn Gly Leu
 405 410 415

Leu Phe Gln Leu Ser Leu Pro Leu Asn Phe Leu Gly Thr Val Tyr Arg
 420 425 430

Glu Thr Arg Gln Ala Leu Ile Asp Met Asn Thr Leu Phe Thr Leu Leu
 435 440 445

Lys Val Asp Thr Gln Ile Lys Asp Lys Val Met Ala Ser Pro Leu Gln
 450 455 460

Ile Thr Pro Gln Thr Ala Thr Val Ala Phe Asp Asn Val His Phe Glu
 465 470 475 480

Tyr Ile Glu Gly Gln Lys Val Leu Ser Gly Ile Ser Phe Glu Val Pro
 485 490 495

Ala Gly Lys Lys Val Ala Ile Val Gly Gly Ser Gly Ser Gly Lys Ser
 500 505 510

Thr Ile Val Arg Leu Leu Phe Arg Phe Tyr Glu Pro Gln Lys Gly Ser
 515 520 525

Ile Tyr Leu Ala Gly Gln Asn Ile Gln Asp Val Ser Leu Glu Ser Leu
 530 535 540

Protein Complexes associated with APP-processing
 Arg Arg Ala Val Gly Val Val Pro Gln Asp Ala Val Leu Phe His Asn
 545 550 555 560

Thr Ile Tyr Tyr Asn Leu Leu Tyr Gly Asn Ile Ser Ala Ser Pro Glu
 565 570 575

Glu Val Tyr Ala Val Ala Lys Leu Ala Gly Leu His Asp Ala Ile Leu
 580 585 590

Arg Met Pro His Gly Tyr Asp Thr Gln Val Gly Glu Arg Gly Leu Lys
 595 600 605

Leu Ser Gly Gly Glu Lys Gln Arg Val Ala Ile Ala Arg Ala Ile Leu
 610 615 620

Lys Asp Pro Pro Val Ile Leu Tyr Asp Glu Ala Thr Ser Ser Leu Asp
 625 630 635 640

Ser Ile Thr Glu Glu Thr Ile Leu Gly Ala Met Lys Asp Val Val Lys
 645 650 655

His Arg Thr Ser Ile Phe Ile Ala His Arg Leu Ser Thr Val Val Asp
 660 665 670

Ala Asp Glu Ile Ile Val Leu Asp Gln Gly Lys Val Ala Glu Arg Gly
 675 680 685

Thr His His Gly Leu Leu Ala Asn Pro His Ser Ile Tyr Ser Glu Met
 690 695 700

Trp His Thr Gln Ser Ser Arg Val Gln Asn His Asp Asn Pro Lys Trp
 705 710 715 720

Glu Ala Lys Lys Glu Asn Ile Ser Lys Glu Glu Glu Arg Lys Lys Leu
 725 730 735

Gln Glu Glu Ile Val Asn Ser Val Lys Gly Cys Gly Asn Cys Ser Cys
 740 745 750

<210> 32

<211> 463

<212> PRT

<213> Homo sapiens

<400> 32

Met Ala Thr Val Thr Ala Thr Thr Lys Val Pro Glu Ile Arg Asp Val
 1 5 10 15

Protein Complexes associated with APP-processing

Thr Arg Ile Glu Arg Ile Gly Ala His Ser His Ile Arg Gly Leu Gly
 20 25 30

Leu Asp Asp Ala Leu Glu Pro Arg Gln Ala Ser Gln Gly Met Val Gly
 35 40 45

Gln Leu Ala Ala Arg Arg Ala Ala Gly Val Val Leu Glu Met Ile Arg
 50 55 60

Glu Gly Lys Ile Ala Gly Arg Ala Val Leu Ile Ala Gly Gln Pro Gly
 65 70 75 80

Thr Gly Lys Thr Ala Ile Ala Met Gly Met Ala Gln Ala Leu Gly Pro
 85 90 95

Asp Thr Pro Phe Thr Ala Ile Ala Gly Ser Glu Ile Phe Ser Leu Glu
 100 105 110

Met Ser Lys Thr Glu Ala Leu Thr Gln Ala Phe Arg Arg Ser Ile Gly
 115 120 125

Val Arg Ile Lys Glu Glu Thr Glu Ile Ile Glu Gly Glu Val Val Glu
 130 135 140

Ile Gln Ile Asp Arg Pro Ala Thr Gly Thr Gly Ser Lys Val Gly Lys
 145 150 155 160

Leu Thr Leu Lys Thr Thr Glu Met Glu Thr Ile Tyr Asp Leu Gly Thr
 165 170 175

Lys Met Ile Glu Ser Leu Thr Lys Asp Lys Val Gln Ala Gly Asp Val
 180 185 190

Ile Thr Ile Asp Lys Ala Thr Gly Lys Ile Ser Lys Leu Gly Arg Ser
 195 200 205

Phe Thr Arg Ala Arg Asp Tyr Asp Ala Met Gly Ser Gln Thr Lys Phe
 210 215 220

Val Gln Cys Pro Asp Gly Glu Leu Gln Lys Arg Lys Glu Val Val His
 225 230 235 240

Thr Val Ser Leu His Glu Ile Asp Val Ile Asn Ser Arg Thr Gln Gly
 245 250 255

Phe Leu Ala Leu Phe Ser Gly Asp Thr Gly Glu Ile Lys Ser Glu Val
 260 265 270

Arg Glu Gln Ile Asn Ala Lys Val Ala Glu Trp Arg Glu Glu Gly Lys
 275 280 285

Protein Complexes associated with APP-processing

Ala Glu Ile Ile Pro Gly Val Leu Phe Ile Asp Glu Val His Met Leu
 290 295 300

Asp Ile Glu Ser Phe Ser Phe Leu Asn Arg Ala Leu Glu Ser Asp Met
 305 310 315 320

Ala Pro Val Leu Ile Met Ala Thr Asn Arg Gly Ile Thr Arg Ile Arg
 325 330 335

Gly Thr Ser Tyr Gln Ser Pro His Gly Ile Pro Ile Asp Leu Leu Asp
 340 345 350

Arg Leu Leu Ile Val Ser Thr Thr Pro Tyr Ser Glu Lys Asp Thr Lys
 355 360 365

Gln Ile Leu Arg Ile Arg Cys Glu Glu Glu Asp Val Glu Met Ser Glu
 370 375 380

Asp Ala Tyr Thr Val Leu Thr Arg Ile Gly Leu Glu Thr Ser Leu Arg
 385 390 395 400

Tyr Ala Ile Gln Leu Ile Thr Ala Ala Ser Leu Val Cys Arg Lys Arg
 405 410 415

Lys Gly Thr Glu Val Gln Val Asp Asp Ile Lys Arg Val Tyr Ser Leu
 420 425 430

Phe Leu Asp Glu Ser Arg Ser Thr Gln Tyr Met Lys Glu Tyr Gln Asp
 435 440 445

Ala Phe Leu Phe Asn Glu Leu Lys Gly Glu Thr Met Asp Thr Ser
 450 455 460

<210> 33

<211> 710

<212> PRT

<213> Homo sapiens

<400> 33

Met Ser Val Pro Ser Ser Leu Ser Gln Ser Ala Ile Asn Ala Asn Ser
 1 5 10 15

His Gly Gly Pro Ala Leu Ser Leu Pro Leu Pro Leu His Ala Ala His
 20 25 30

Asn Gln Leu Leu Asn Ala Lys Leu Gln Ala Thr Ala Val Gly Pro Lys
 35 40 45

Protein Complexes associated with APP-processing

Asp Leu Arg Ser Ala Met Gly Glu Gly Gly Gly Pro Glu Pro Gly Pro
 50 55 60

Ala Asn Ala Lys Trp Leu Lys Glu Gly Gln Asn Gln Leu Arg Arg Ala
 65 70 75 80

Ala Thr Ala His Arg Asp Gln Asn Arg Asn Val Thr Leu Thr Leu Ala
 85 90 95

Glu Glu Ala Ser Gln Glu Pro Glu Met Ala Pro Leu Gly Pro Lys Gly
 100 105 110

Leu Ile His Leu Tyr Ser Glu Leu Glu Leu Ser Ala His Asn Ala Ala
 115 120 125

Asn Arg Gly Leu Arg Gly Pro Gly Leu Ile Ile Ser Thr Gln Glu Gln
 130 135 140

Gly Pro Asp Glu Gly Glu Glu Lys Ala Ala Gly Glu Ala Glu Glu Glu
 145 150 155 160

Glu Glu Asp Asp Asp Glu Glu Glu Glu Asp Leu Ser Ser Pro
 165 170 175

Pro Gly Leu Pro Glu Pro Leu Glu Ser Val Glu Ala Pro Pro Arg Pro
 180 185 190

Gln Ala Leu Thr Asp Gly Pro Arg Glu His Ser Lys Ser Ala Ser Leu
 195 200 205

Leu Phe Gly Met Arg Asn Ser Ala Ala Ser Asp Glu Asp Ser Ser Trp
 210 215 220

Ala Thr Leu Ser Gln Gly Ser Pro Ser Tyr Gly Ser Pro Glu Asp Thr
 225 230 235 240

Asp Ser Phe Trp Asn Pro Asn Ala Phe Glu Thr Asp Ser Asp Leu Pro
 245 250 255

Ala Gly Trp Met Arg Val Gln Asp Thr Ser Gly Thr Tyr Tyr Trp His
 260 265 270

Ile Pro Thr Gly Thr Thr Gln Trp Glu Pro Pro Gly Arg Ala Ser Pro
 275 280 285

Ser Gln Gly Ser Ser Pro Gln Glu Glu Ser Gln Leu Thr Trp Thr Gly
 290 295 300

Phe Ala His Gly Glu Gly Phe Glu Asp Gly Glu Phe Trp Lys Asp Glu
 305 310 315 320

Protein Complexes associated with APP-processing

Pro Ser Asp Glu Ala Pro Met Glu Leu Gly Leu Lys Glu Pro Glu Glu
 325 330 335

Gly Thr Leu Thr Phe Pro Ala Gln Ser Leu Ser Pro Glu Pro Leu Pro
 340 345 350

Gln Glu Glu Glu Lys Leu Pro Pro Arg Asn Thr Asn Pro Gly Ile Lys
 355 360 365

Cys Phe Ala Val Arg Ser Leu Gly Trp Val Glu Met Thr Glu Glu Glu
 370 375 380

Leu Ala Pro Gly Arg Ser Ser Val Ala Val Asn Asn Cys Ile Arg Gln
 385 390 395 400

Leu Ser Tyr His Lys Asn Asn Leu His Asp Pro Met Ser Gly Gly Trp
 405 410 415

Gly Glu Gly Lys Asp Leu Leu Leu Gln Leu Glu Asp Glu Thr Leu Lys
 420 425 430

Leu Val Glu Pro Gln Ser Gln Ala Leu Leu His Ala Gln Pro Ile Ile
 435 440 445

Ser Ile Arg Val Trp Gly Val Gly Arg Asp Ser Gly Arg Glu Arg Asp
 450 455 460

Phe Ala Tyr Val Ala Arg Asp Lys Leu Thr Gln Met Leu Lys Cys His
 465 470 475 480

Val Phe Arg Cys Glu Ala Pro Ala Lys Asn Ile Ala Thr Ser Leu His
 485 490 495

Glu Ile Cys Ser Lys Ile Met Ala Glu Arg Arg Asn Ala Arg Cys Leu
 500 505 510

Val Asn Gly Leu Ser Leu Asp His Ser Lys Leu Val Asp Val Pro Phe
 515 520 525

Gln Val Glu Phe Pro Ala Pro Lys Asn Glu Leu Val Gln Lys Phe Gln
 530 535 540

Val Tyr Tyr Leu Gly Asn Val Pro Val Ala Lys Pro Val Gly Val Asp
 545 550 555 560

Val Ile Asn Gly Ala Leu Glu Ser Val Leu Ser Ser Ser Ser Arg Glu
 565 570 575

Gln Trp Thr Pro Ser His Val Ser Val Ala Pro Ala Thr Leu Thr Ile
 580 585 590

Protein Complexes associated with APP-processing
 Leu His Gln Gln Thr Glu Ala Val Leu Gly Glu Cys Arg Val Arg Phe
 595 600 605

Leu Ser Phe Leu Ala Val Gly Arg Asp Val His Thr Phe Ala Phe Ile
 610 615 620

Met Ala Ala Gly Pro Ala Ser Phe Cys Cys His Met Phe Trp Cys Glu
 625 630 635 640

Pro Asn Ala Ala Ser Leu Ser Glu Ala Val Gln Ala Ala Cys Met Leu
 645 650 655

Arg Tyr Gln Lys Cys Leu Asp Ala Arg Ser Gln Ala Ser Thr Ser Cys
 660 665 670

Leu Pro Ala Pro Pro Ala Glu Ser Val Ala Arg Arg Val Gly Trp Thr
 675 680 685

Val Arg Arg Gly Val Gln Ser Leu Trp Gly Ser Leu Lys Pro Lys Arg
 690 695 700

Leu Gly Ala His Thr Pro
 705 710

<210> 34

<211> 443

<212> PRT

<213> Homo sapiens

<400> 34

Met Gln Arg Arg Asp Asp Pro Ala Ala Arg Met Ser Arg Ser Ser Gly
 1 5 10 15

Arg Ser Gly Ser Met Asp Pro Ser Gly Ala His Pro Ser Val Arg Gln
 20 25 30

Thr Pro Ser Arg Gln Pro Pro Leu Pro His Arg Ser Arg Gly Gly Gly
 35 40 45

Gly Gly Ser Arg Gly Gly Ala Arg Ala Ser Pro Ala Thr Gln Pro Pro
 50 55 60

Pro Leu Leu Pro Pro Ser Ala Thr Gly Pro Asp Ala Thr Val Gly Gly
 65 70 75 80

Pro Ala Pro Thr Pro Leu Leu Pro Pro Ser Ala Thr Ala Ser Val Lys
 85 90 95

Protein Complexes associated with APP-processing

Met Glu Pro Glu Asn Lys Tyr Leu Pro Glu Leu Met Ala Glu Lys Asp
100 105 110

Ser Leu Asp Pro Ser Phe Thr His Ala Met Gln Leu Leu Thr Ala Glu
115 120 125

Ile Glu Lys Ile Gln Lys Gly Asp Ser Lys Lys Asp Asp Glu Glu Asn
130 135 140

Tyr Leu Asp Leu Phe Ser His Lys Asn Met Lys Leu Lys Glu Arg Val
145 150 155 160

Leu Ile Pro Val Lys Gln Tyr Pro Lys Phe Asn Phe Val Gly Lys Ile
165 170 175

Leu Gly Pro Gln Gly Asn Thr Ile Lys Arg Leu Gln Glu Glu Thr Gly
180 185 190

Ala Lys Ile Ser Val Leu Gly Lys Gly Ser Met Arg Asp Lys Ala Lys
195 200 205

Glu Glu Glu Leu Arg Lys Gly Gly Asp Pro Lys Tyr Ala His Leu Asn
210 215 220

Met Asp Leu His Val Phe Ile Glu Val Phe Gly Pro Pro Cys Glu Ala
225 230 235 240

Tyr Ala Leu Met Ala His Ala Met Glu Glu Val Lys Lys Phe Leu Val
245 250 255

Pro Asp Met Met Asp Asp Ile Cys Gln Glu Gln Phe Leu Glu Leu Ser
260 265 270

Tyr Leu Asn Gly Val Pro Glu Pro Ser Arg Gly Arg Gly Val Pro Val
275 280 285

Arg Gly Arg Gly Ala Ala Pro Pro Pro Pro Pro Val Pro Arg Gly Arg
290 295 300

Gly Val Gly Pro Pro Arg Gly Ala Leu Val Arg Gly Thr Pro Val Arg
305 310 315 320

Gly Ala Ile Thr Arg Gly Ala Thr Val Thr Arg Gly Val Pro Pro Pro
325 330 335

Pro Thr Val Arg Gly Ala Pro Ala Pro Arg Ala Arg Thr Ala Gly Ile
340 345 350

Gln Arg Ile Pro Leu Pro Pro Pro Pro Ala Pro Glu Thr Tyr Glu Glu
355 360 365

Protein Complexes associated with APP-processing
 Tyr Gly Tyr Asp Asp Thr Tyr Ala Glu Gln Ser Tyr Glu Gly Tyr Glu
 370 375 380

Gly Tyr Tyr Ser Gln Ser Gln Gly Asp Ser Glu Tyr Tyr Asp Tyr Gly
 385 390 395 400

His Gly Glu Val Gln Asp Ser Tyr Glu Ala Tyr Gly Gln Asp Asp Trp
 405 410 415

Asn Gly Thr Arg Pro Ser Leu Lys Ala Pro Pro Ala Arg Pro Val Lys
 420 425 430

Gly Ala Tyr Arg Glu His Pro Tyr Gly Arg Tyr
 435 440

<210> 35

<211> 266

<212> PRT

<213> Homo sapiens

<400> 35

Met Val Lys Val Thr Phe Asn Ser Ala Leu Ala Gln Lys Glu Ala Lys
 1 5 10 15

Lys Asp Glu Pro Lys Ser Gly Glu Glu Ala Leu Ile Ile Pro Pro Asp
 20 25 30

Ala Val Ala Val Asp Cys Lys Asp Pro Asp Asp Val Val Pro Val Gly
 35 40 45

Gln Arg Arg Ala Trp Cys Trp Cys Met Cys Phe Gly Leu Ala Phe Met
 50 55 60

Leu Ala Gly Val Ile Leu Gly Gly Ala Tyr Leu Tyr Lys Tyr Phe Ala
 65 70 75 80

Leu Gln Pro Asp Asp Val Tyr Tyr Cys Gly Ile Lys Tyr Ile Lys Asp
 85 90 95

Asp Val Ile Leu Asn Glu Pro Ser Ala Asp Ala Pro Ala Ala Leu Tyr
 100 105 110

Gln Thr Ile Glu Glu Asn Ile Lys Ile Phe Glu Glu Glu Glu Val Glu
 115 120 125

Phe Ile Ser Val Pro Val Pro Glu Phe Ala Asp Ser Asp Pro Ala Asn
 130 135 140

Protein Complexes associated with APP-processing

Ile Val His Asp Phe Asn Lys Lys Leu Thr Ala Tyr Leu Asp Leu Asn
 145 150 155 160

Leu Asp Lys Cys Tyr Val Ile Pro Leu Asn Thr Ser Ile Val Met Pro
 165 170 175

Pro Arg Asn Leu Leu Glu Leu Leu Ile Asn Ile Lys Ala Gly Thr Tyr
 180 185 190

Leu Pro Gln Ser Tyr Leu Ile His Glu His Met Val Ile Thr Asp Arg
 195 200 205

Ile Glu Asn Ile Asp His Leu Gly Phe Phe Ile Tyr Arg Leu Cys His
 210 215 220

Asp Lys Glu Thr Tyr Lys Leu Gln Arg Arg Glu Thr Ile Lys Gly Ile
 225 230 235 240

Gln Lys Arg Glu Ala Ser Asn Cys Phe Ala Ile Arg His Phe Glu Asn
 245 250 255

Lys Phe Ala Val Glu Thr Leu Ile Cys Ser
 260 265

<210> 36

<211> 333

<212> PRT

<213> Homo sapiens

<400> 36

Met Ala Ser Arg Pro Arg Pro Arg Thr Pro Ser Arg Gly Pro Ser Asp
 1 5 10 15

Leu Arg Phe Arg Gly Glu Ala Gly Leu Arg Arg Val Phe Leu Lys Lys
 20 25 30

Ala Gly Val Arg Val Arg Pro Ala Asp Lys Arg Ala Ala Gly Ser Arg
 35 40 45

Val Gly Cys Pro Trp His Arg Ala Glu Pro Pro Leu Gly Thr Arg Glu
 50 55 60

Gln Gln Gly Phe Arg Lys Arg Arg Glu Arg Trp Thr Gly Gly Arg Pro
 65 70 75 80

Gly Phe Ala Gln Ala Pro Pro Leu Gly Gly Pro Ala Gln Gly Ala Leu
 85 90 95

Protein Complexes associated with APP-processing
 Arg Gln Phe Pro Cys Asp Val Ala Val Gly Phe Thr Gln Glu Glu Trp
 100 105 110

Gln His Leu Asp Ser Ala Gln Arg Thr Pro Tyr Arg Asp Met Met Leu
 115 120 125

Glu Asn Tyr Ser Leu Leu Leu Ser Val Gly Tyr Cys Ile Thr Lys Pro
 130 135 140

Glu Val Val Cys Lys Leu Glu His Gly Gln Val Leu Trp Ile Leu Glu
 145 150 155 160

Glu Glu Ser Pro Ser Gln Ser His Leu Asp Cys Cys Ile Asp Asp Asp
 165 170 175

Leu Met Glu Lys Arg Gln Glu Asn Gln Asp Gln His Leu Gln Lys Val
 180 185 190

Asp Phe Val Asn Asn Lys Thr Leu Thr Met Asp Arg Asn Gly Val Leu
 195 200 205

Gly Lys Thr Phe Ser Leu Asp Thr Asn Pro Ile Leu Ser Arg Lys Ile
 210 215 220

Arg Gly Asn Cys Asp Ser Ser Gly Met Asn Leu Asn Asn Ile Ser Glu
 225 230 235 240

Leu Ile Ile Ser Asn Arg Ser Ser Phe Val Arg Asn Pro Ala Glu Cys
 245 250 255

Asn Val Arg Gly Lys Phe Leu Leu Cys Met Lys Arg Glu Asn Pro Tyr
 260 265 270

Ala Arg Gly Lys Pro Leu Glu Tyr Asp Gly Asn Gly Lys Ala Val Ser
 275 280 285

Gln Asn Glu Asp Leu Phe Arg His Gln Tyr Ile Gln Thr Leu Lys Gln
 290 295 300

Cys Phe Glu Tyr Asn Gln Cys Gly Lys Ala Phe His Glu Glu Ala Ala
 305 310 315 320

Cys Ser Thr His Lys Arg Val Cys Ser Trp Glu Thr Leu
 325 330

<210> 37

<211> 1027

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 37

Asp Val Ile Val Asp Ile Asn Gly Asn Cys Val Leu Gly His Thr His
 1 5 10 15

Ala Asp Val Val Gln Met Phe Gln Leu Val Pro Val Asn Gln Tyr Val
 20 25 30

Asn Leu Thr Leu Cys Arg Gly Tyr Pro Leu Pro Asp Asp Ser Glu Asp
 35 40 45

Pro Val Val Asp Ile Val Ala Ala Thr Pro Val Ile Asn Gly Gln Ser
 50 55 60

Leu Thr Lys Gly Glu Thr Cys Met Asn Pro Gln Asp Phe Lys Pro Gly
 65 70 75 80

Ala Met Val Leu Glu Gln Asn Gly Lys Ser Gly His Thr Leu Thr Gly
 85 90 95

Asp Gly Leu Asn Gly Pro Ser Asp Ala Ser Glu Gln Arg Val Ser Met
 100 105 110

Ala Ser Ser Gly Ser Ser Gln Pro Glu Leu Val Thr Ile Pro Leu Ile
 115 120 125

Lys Gly Pro Lys Gly Phe Gly Phe Ala Ile Ala Asp Ser Pro Thr Gly
 130 135 140

Gln Lys Val Lys Met Ile Leu Asp Ser Gln Trp Cys Gln Gly Leu Gln
 145 150 155 160

Lys Gly Asp Ile Ile Lys Glu Ile Tyr His Gln Asn Val Gln Asn Leu
 165 170 175

Thr His Leu Gln Val Val Glu Val Leu Lys Gln Phe Pro Val Gly Ala
 180 185 190

Asp Val Pro Leu Leu Ile Leu Arg Gly Gly Pro Pro Ser Pro Thr Lys
 195 200 205

Thr Ala Lys Met Lys Thr Asp Lys Lys Glu Asn Ala Gly Ser Leu Glu
 210 215 220

Ala Ile Asn Glu Pro Ile Pro Gln Pro Met Pro Phe Pro Pro Ser Ile
 225 230 235 240

Ile Arg Ser Gly Ser Pro Lys Leu Asp Pro Ser Glu Val Tyr Leu Lys
 245 250 255

Protein Complexes associated with APP-processing
 Ser Lys Thr Leu Tyr Glu Asp Lys Pro Pro Asn Thr Lys Asp Leu Asp
 260 265 270

Val Phe Leu Arg Lys Gln Glu Ser Gly Phe Gly Phe Arg Val Leu Gly
 275 280 285

Gly Asp Gly Pro Asp Gln Ser Ile Tyr Ile Gly Ala Ile Ile Pro Leu
 290 295 300

Gly Ala Ala Glu Lys Asp Gly Arg Leu Arg Ala Ala Asp Glu Leu Met
 305 310 315 320

Cys Ile Asp Gly Ile Pro Val Lys Gly Lys Ser His Lys Gln Val Leu
 325 330 335

Asp Leu Met Thr Thr Ala Ala Arg Asn Gly His Val Leu Leu Thr Val
 340 345 350

Arg Arg Lys Ile Phe Tyr Gly Glu Lys Gln Pro Glu Asp Asp Ser Ser
 355 360 365

Gln Ala Phe Ile Ser Thr Gln Asn Gly Ser Pro Arg Leu Asn Arg Ala
 370 375 380

Glu Val Pro Ala Arg Pro Ala Pro Gln Glu Pro Tyr Asp Val Val Leu
 385 390 395 400

Gln Arg Lys Glu Asn Glu Gly Phe Gly Phe Val Ile Leu Thr Ser Lys
 405 410 415

Asn Lys Pro Pro Pro Gly Val Ile Pro His Lys Ile Gly Arg Val Ile
 420 425 430

Glu Gly Ser Pro Ala Asp Arg Cys Gly Lys Leu Lys Val Gly Asp His
 435 440 445

Ile Ser Ala Val Asn Gly Gln Ser Ile Val Glu Leu Ser His Asp Asn
 450 455 460

Ile Val Gln Leu Ile Lys Asp Ala Gly Val Thr Val Thr Leu Thr Val
 465 470 475 480

Ile Ala Glu Glu Glu His His Gly Pro Pro Ser Gly Thr Asn Ser Ala
 485 490 495

Arg Gln Ser Pro Ala Leu Gln His Arg Pro Met Gly Gln Ser Gln Ala
 500 505 510

Asn His Ile Pro Gly Asp Arg Ser Ala Leu Glu Gly Glu Ile Gly Lys
 515 520 525

Protein Complexes associated with APP-processing

Asp Val Ser Thr Ser Tyr Arg His Ser Trp Ser Asp His Lys His Leu
 530 535 540

Ala Gln Pro Asp Thr Ala Val Ile Ser Val Val Gly Ser Arg His Asn
 545 550 555 560

Gln Asn Leu Gly Cys Tyr Pro Val Glu Leu Glu Arg Gly Pro Arg Gly
 565 570 575

Phe Gly Phe Ser Leu Arg Gly Gly Lys Glu Tyr Asn Met Gly Leu Phe
 580 585 590

Ile Leu Arg Leu Ala Glu Asp Gly Pro Ala Ile Lys Asp Gly Arg Ile
 595 600 605

His Val Gly Asp Gln Ile Val Glu Ile Asn Gly Glu Pro Thr Gln Gly
 610 615 620

Ile Thr His Thr Arg Ala Ile Glu Leu Ile Gln Ala Gly Gly Asn Lys
 625 630 635 640

Val Leu Leu Leu Leu Arg Pro Gly Thr Gly Leu Ile Pro Asp His Gly
 645 650 655

Asp Trp Asp Ile Asn Asn Pro Ser Ser Ser Asn Val Ile Tyr Asp Glu
 660 665 670

Gln Ser Pro Leu Pro Pro Ser Ser His Phe Ala Ser Ile Phe Glu Glu
 675 680 685

Ser His Val Pro Val Ile Glu Glu Ser Leu Arg Val Gln Ile Cys Glu
 690 695 700

Lys Ala Glu Glu Leu Lys Asp Ile Val Pro Glu Lys Lys Ser Thr Leu
 705 710 715 720

Asn Glu Asn Gln Pro Glu Ile Lys His Gln Ser Leu Leu Gln Lys Asn
 725 730 735

Val Ser Lys Arg Asp Pro Pro Ser Ser His Gly His Ser Asn Lys Lys
 740 745 750

Asn Leu Leu Lys Val Glu Asn Gly Val Thr Arg Arg Gly Arg Ser Val
 755 760 765

Ser Pro Lys Lys Pro Ala Ser Gln His Ser Glu Glu His Leu Asp Lys
 770 775 780

Ile Pro Ser Pro Leu Lys Asn Asn Pro Lys Arg Arg Pro Arg Asp Gln
 785 790 795 800

Protein Complexes associated with APP-processing
 Ser Leu Ser Pro Ser Lys Gly Glu Asn Lys Ser Cys Gln Val Ser Thr
 805 810 815

Arg Ala Gly Ser Gly Gln Asp Gln Cys Arg Lys Ser Arg Gly Arg Ser
 820 825 830

Ala Ser Pro Lys Lys Gln Gln Lys Ile Glu Gly Ser Lys Ala Pro Ser
 835 840 845

Asn Ala Glu Ala Lys Leu Leu Glu Gly Lys Ser Arg Arg Ile Ala Gly
 850 855 860

Tyr Thr Gly Ser Asn Ala Glu Gln Ile Pro Asp Gly Lys Glu Lys Ser
 865 870 875 880

Asp Val Ile Arg Lys Asp Ala Lys Gln Asn Gln Leu Glu Lys Ser Arg
 885 890 895

Thr Arg Ser Pro Glu Lys Lys Ile Lys Arg Met Val Glu Lys Ser Leu
 900 905 910

Pro Ser Lys Met Thr Asn Lys Thr Thr Ser Lys Glu Val Ser Glu Asn
 915 920 925

Glu Lys Gly Lys Lys Val Thr Thr Gly Glu Thr Ser Ser Ser Asn Asp
 930 935 940

Lys Ile Gly Glu Asn Val Gln Leu Ser Glu Lys Arg Leu Lys Gln Glu
 945 950 955 960

Pro Glu Glu Lys Val Val Ser Asn Lys Thr Glu Asp His Lys Gly Lys
 965 970 975

Glu Leu Glu Ala Ala Asp Lys Asn Lys Glu Thr Gly Arg Phe Lys Pro
 980 985 990

Glu Ser Ser Ser Pro Val Lys Lys Thr Leu Ile Thr Pro Gly Pro Trp
 995 1000 1005

Lys Val Pro Ser Gly Asn Lys Val Thr Gly Thr Ile Gly Met Ala
 1010 1015 1020

Glu Lys Arg Gln
 1025

<210> 38

<211> 447

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 38

Met Ala Gly Ala Gly Gly Gly Asn Asp Ile Gln Trp Cys Phe Ser Gln
 1 5 10 15

Val Lys Gly Ala Val Asp Asp Asp Val Ala Glu Ala Asp Ile Ile Ser
 20 25 30

Thr Val Glu Phe Asn His Ser Gly Glu Leu Leu Ala Thr Gly Asp Lys
 35 40 45

Gly Gly Arg Val Val Ile Phe Gln Gln Glu Gln Glu Asn Lys Ile Gln
 50 55 60

Ser His Ser Arg Gly Glu Tyr Asn Val Tyr Ser Thr Phe Gln Ser His
 65 70 75 80

Glu Pro Glu Phe Asp Tyr Leu Lys Ser Leu Glu Ile Glu Glu Lys Ile
 85 90 95

Asn Lys Ile Arg Trp Leu Pro Gln Lys Asn Ala Ala Gln Phe Leu Leu
 100 105 110

Ser Thr Asn Asp Lys Thr Ile Lys Leu Trp Lys Ile Ser Glu Arg Asp
 115 120 125

Lys Arg Pro Glu Gly Tyr Asn Leu Lys Glu Glu Asp Gly Arg Tyr Arg
 130 135 140

Asp Pro Thr Thr Val Thr Thr Leu Arg Val Pro Val Phe Arg Pro Met
 145 150 155 160

Asp Leu Met Val Glu Ala Ser Pro Arg Arg Ile Phe Ala Asn Ala His
 165 170 175

Thr Tyr His Ile Asn Ser Ile Ser Ile Asn Ser Asp Tyr Glu Thr Tyr
 180 185 190

Leu Ser Ala Asp Asp Leu Arg Ile Asn Leu Trp His Leu Glu Ile Thr
 195 200 205

Asp Arg Ser Phe Asn Ile Val Asp Ile Lys Pro Ala Asn Met Glu Glu
 210 215 220

Leu Thr Glu Val Ile Thr Ala Ala Glu Phe His Pro Asn Ser Cys Asn
 225 230 235 240

Thr Phe Val Tyr Ser Ser Ser Lys Gly Thr Ile Arg Leu Cys Asp Met
 245 250 255

Protein Complexes associated with APP-processing

Arg Ala Ser Ala Leu Cys Asp Arg His Ser Lys Leu Phe Glu Glu Pro
 260 265 270

Glu Asp Pro Ser Asn Arg Ser Phe Phe Ser Glu Ile Ile Ser Ser Ile
 275 280 285

Ser Asp Val Lys Phe Ser His Ser Gly Arg Tyr Met Met Thr Arg Asp
 290 295 300

Tyr Leu Ser Val Lys Ile Trp Asp Leu Asn Met Glu Asn Arg Pro Val
 305 310 315 320

Glu Thr Tyr Gln Val His Glu Tyr Leu Arg Ser Lys Leu Cys Ser Leu
 325 330 335

Tyr Glu Asn Asp Cys Ile Phe Asp Lys Phe Glu Cys Cys Trp Asn Gly
 340 345 350

Ser Asp Ser Val Val Met Thr Gly Ser Tyr Asn Asn Phe Phe Arg Met
 355 360 365

Phe Asp Arg Asn Thr Lys Arg Asp Ile Thr Leu Glu Ala Ser Arg Glu
 370 375 380

Asn Asn Lys Pro Arg Thr Val Leu Lys Pro Arg Lys Val Cys Ala Ser
 385 390 395 400

Gly Lys Arg Lys Lys Asp Glu Ile Ser Val Asp Ser Leu Asp Phe Asn
 405 410 415

Lys Lys Ile Leu His Thr Ala Trp His Pro Lys Glu Asn Ile Ile Ala
 420 425 430

Val Ala Thr Thr Asn Asn Leu Tyr Ile Phe Gln Asp Lys Val Asn
 435 440 445

<210> 39

<211> 1148

<212> PRT

<213> Homo sapiens

<400> 39

Met Glu Lys Ile Arg Val Cys Val Arg Lys Arg Pro Leu Gly Met Arg
 1 5 10 15

Glu Val Arg Arg Gly Glu Ile Asn Ile Ile Thr Val Glu Asp Lys Glu
 20 25 30

Protein Complexes associated with APP-processing

Thr Leu Leu Val His Glu Lys Lys Glu Ala Val Asp Leu Thr Gln Tyr
 35 40 45

Ile Leu Gln His Val Phe Tyr Phe Asp Glu Val Phe Gly Glu Ala Cys
 50 55 60

Thr Asn Gln Asp Val Tyr Met Lys Thr Thr His Pro Leu Ile Gln His
 65 70 75 80

Ile Phe Asn Gly Gly Asn Ala Thr Cys Phe Ala Tyr Gly Gln Thr Gly
 85 90 95

Ala Gly Lys Thr Tyr Thr Met Ile Gly Thr His Glu Asn Pro Gly Leu
 100 105 110

Tyr Ala Leu Ala Ala Lys Asp Ile Phe Arg Gln Leu Glu Val Ser Gln
 115 120 125

Pro Arg Lys His Leu Phe Val Trp Ile Ser Phe Tyr Glu Ile Tyr Cys
 130 135 140

Gly Gln Leu Tyr Asp Leu Leu Asn Arg Arg Lys Arg Leu Phe Ala Arg
 145 150 155 160

Glu Asp Ser Lys His Met Val Gln Ile Val Gly Leu Gln Glu Leu Gln
 165 170 175

Val Asp Ser Val Glu Leu Leu Leu Glu Val Ile Leu Lys Gly Ser Lys
 180 185 190

Glu Arg Ser Thr Gly Ala Thr Gly Val Asn Ala Asp Ser Ser Arg Ser
 195 200 205

His Ala Val Ile Gln Ile Gln Ile Lys Asp Ser Ala Lys Arg Thr Phe
 210 215 220

Gly Arg Ile Ser Phe Ile Asp Leu Ala Gly Ser Glu Arg Ala Ala Asp
 225 230 235 240

Ala Arg Asp Ser Asp Arg Gln Thr Lys Met Glu Gly Ala Glu Ile Asn
 245 250 255

Gln Ser Leu Leu Ala Leu Lys Glu Cys Ile Arg Ala Leu Asp Gln Glu
 260 265 270

His Thr His Thr Pro Phe Arg Gln Ser Lys Leu Thr Gln Val Leu Lys
 275 280 285

Asp Ser Phe Ile Gly Asn Ala Lys Thr Cys Met Ile Ala Asn Ile Ser
 290 295 300

Protein Complexes associated with APP-processing
 Pro Ser His Val Ala Thr Glu His Thr Leu Asn Thr Leu Arg Tyr Ala
 305 310 315 320

Asp Arg Val Lys Glu Leu Lys Lys Gly Ile Lys Cys Cys Thr Ser Val
 325 330 335

Thr Ser Arg Asn Arg Thr Ser Gly Asn Ser Ser Pro Lys Arg Ile Gln
 340 345 350

Ser Ser Pro Gly Ala Leu Ser Glu Asp Lys Cys Ser Pro Lys Lys Val
 355 360 365

Lys Leu Gly Phe Gln Gln Ser Leu Thr Val Ala Ala Pro Gly Ser Thr
 370 375 380

Arg Gly Lys Val His Pro Leu Thr Ser His Pro Pro Asn Ile Pro Phe
 385 390 395 400

Thr Ser Ala Pro Lys Val Ser Gly Lys Arg Gly Gly Ser Arg Gly Ser
 405 410 415

Pro Ser Gln Glu Trp Val Ile His Ala Ser Pro Val Lys Gly Thr Val
 420 425 430

Arg Ser Gly His Val Ala Lys Lys Lys Pro Glu Glu Ser Ala Pro Leu
 435 440 445

Cys Ser Glu Lys Asn Arg Met Gly Asn Lys Thr Val Leu Gly Trp Glu
 450 455 460

Ser Arg Ala Ser Gly Pro Gly Glu Gly Leu Val Arg Gly Lys Leu Ser
 465 470 475 480

Thr Lys Cys Lys Lys Val Gln Thr Val Gln Pro Val Gln Lys Gln Leu
 485 490 495

Val Ser Arg Val Glu Leu Ser Phe Gly Asn Ala His His Arg Ala Glu
 500 505 510

Tyr Ser Gln Asp Ser Gln Arg Gly Thr Pro Ala Arg Pro Ala Ser Glu
 515 520 525

Ala Trp Thr Asn Ile Pro Pro His Gln Lys Glu Arg Glu Glu His Leu
 530 535 540

Arg Phe Tyr His Gln Gln Phe Gln Gln Pro Pro Leu Leu Gln Gln Lys
 545 550 555 560

Leu Lys Tyr Gln Pro Leu Lys Arg Ser Leu Arg Gln Tyr Arg Pro Pro
 565 570 575

Protein Complexes associated with APP-processing

Glu Gly Gln Leu Thr Asn Glu Thr Pro Pro Leu Phe His Ser Tyr Ser
 580 585 590

Glu Asn His Asp Gly Ala Gln Val Glu Glu Leu Asp Asp Ser Asp Phe
 595 600 605

Ser Glu Asp Ser Phe Ser His Ile Ser Ser Gln Arg Ala Thr Lys Gln
 610 615 620

Arg Asn Thr Leu Glu Asn Ser Glu Asp Ser Phe Phe Leu His Gln Thr
 625 630 635 640

Trp Gly Gln Gly Pro Glu Lys Gln Val Ala Glu Arg Gln Gln Ser Leu
 645 650 655

Phe Ser Ser Pro Arg Thr Gly Asp Lys Lys Asp Leu Thr Lys Ser Trp
 660 665 670

Val Asp Ser Arg Asp Pro Ile Asn His Arg Arg Ala Ala Leu Asp His
 675 680 685

Ser Cys Ser Pro Ser Lys Gly Pro Val Asp Trp Ser Arg Glu Asn Ser
 690 695 700

Thr Ser Ser Gly Pro Ser Pro Arg Asp Ser Leu Ala Glu Lys Pro Tyr
 705 710 715 720

Cys Ser Gln Val Asp Phe Ile Tyr Arg Gln Glu Arg Gly Gly Gly Ser
 725 730 735

Ser Phe Asp Leu Arg Lys Asp Ala Ser Gln Ser Glu Val Ser Gly Glu
 740 745 750

Asn Glu Gly Asn Leu Pro Ser Pro Glu Glu Asp Gly Phe Thr Ile Ser
 755 760 765

Leu Ser His Val Ala Val Pro Gly Ser Pro Asp Gln Arg Asp Thr Val
 770 775 780

Thr Thr Pro Leu Arg Glu Val Ser Ala Asp Gly Pro Ile Gln Val Thr
 785 790 795 800

Ser Thr Val Lys Asn Gly His Ala Val Pro Gly Glu Asp Pro Arg Gly
 805 810 815

Gln Leu Gly Thr His Ala Glu Tyr Ala Ser Gly Leu Met Ser Pro Leu
 820 825 830

Thr Met Ser Leu Leu Glu Asn Pro Asp Asn Glu Gly Ser Pro Pro Ser
 835 840 845

Protein Complexes associated with APP-processing

Glu Gln Leu Val Gln Asp Gly Ala Thr His Ser Leu Val Ala Glu Ser
850 855 860

Thr Gly Gly Pro Val Val Ser His Thr Val Pro Ser Gly Asp Gln Glu
865 870 875 880

Ala Ala Leu Pro Val Ser Ser Ala Thr Arg His Leu Trp Leu Ser Ser
885 890 895

Ser Pro Pro Asp Asn Lys Pro Gly Gly Asp Leu Pro Ala Leu Ser Pro
900 905 910

Ser Pro Ile Arg Gln His Pro Ala Asp Lys Leu Pro Ser Arg Glu Ala
915 920 925

Asp Leu Gly Glu Ala Cys Gln Ser Arg Glu Thr Val Leu Phe Ser His
930 935 940

Glu His Met Gly Ser Glu Gln Tyr Asp Ala Asp Ala Glu Glu Thr Gly
945 950 955 960

Leu Asp Gly Ser Trp Gly Phe Pro Gly Lys Pro Phe Thr Thr Ile His
965 970 975

Met Gly Val Pro His Ser Gly Pro Thr Leu Thr Pro Arg Thr Gly Ser
980 985 990

Ser Asp Val Ala Asp Gln Leu Trp Ala Gln Glu Arg Lys His Pro Thr
995 1000 1005

Arg Leu Gly Trp Gln Glu Phe Gly Leu Ser Thr Asp Pro Ile Lys
1010 1015 1020

Leu Pro Cys Asn Ser Glu Asn Val Thr Trp Leu Lys Pro Arg Pro
1025 1030 1035

Ile Ser Arg Cys Leu Ala Arg Pro Ser Ser Pro Leu Val Pro Ser
1040 1045 1050

Cys Ser Pro Lys Thr Ala Gly Thr Leu Arg Gln Pro Thr Leu Glu
1055 1060 1065

Gln Ala Gln Gln Val Val Ile Arg Ala His Gln Glu Gln Leu Asp
1070 1075 1080

Glu Met Ala Glu Leu Gly Phe Lys Glu Glu Thr Leu Met Ser Gln
1085 1090 1095

Leu Ala Ser Asn Asp Phe Glu Asp Phe Val Thr Gln Leu Asp Glu
1100 1105 1110

Protein Complexes associated with APP-processing
 Ile Met Val Leu Lys Ser Lys Cys Ile Gln Ser Leu Arg Ser Gln
 1115 1120 1125

Leu Gln Leu Tyr Leu Thr Cys His Gly Pro Thr Ala Ala Pro Glu
 1130 1135 1140

Gly Thr Val Pro Ser
 1145

<210> 40

<211> 418

<212> PRT

<213> Homo sapiens

<400> 40

Met Ala Thr Ser Glu Gln Ser Ile Cys Gln Ala Arg Ala Ser Val Met
 1 5 10 15

Val Tyr Asp Asp Thr Ser Lys Lys Trp Val Pro Ile Lys Pro Gly Gln
 20 25 30

Gln Gly Phe Ser Arg Ile Asn Ile Tyr His Asn Thr Ala Ser Asn Thr
 35 40 45

Phe Arg Val Val Gly Val Lys Leu Gln Asp Gln Gln Val Val Ile Asn
 50 55 60

Tyr Ser Ile Val Lys Gly Leu Lys Tyr Asn Gln Ala Thr Pro Thr Phe
 65 70 75 80

His Gln Trp Arg Asp Ala Arg Gln Val Tyr Gly Leu Asn Phe Ala Ser
 85 90 95

Lys Glu Glu Ala Thr Thr Phe Ser Asn Ala Met Leu Phe Ala Leu Asn
 100 105 110

Ile Met Asn Ser Gln Glu Gly Gly Pro Ser Ser Gln Arg Gln Val Gln
 115 120 125

Asn Gly Pro Ser Pro Asp Glu Met Asp Ile Gln Arg Arg Gln Val Met
 130 135 140

Glu Gln His Gln Gln Gln Arg Gln Glu Ser Leu Glu Arg Arg Thr Ser
 145 150 155 160

Ala Thr Gly Pro Ile Leu Pro Pro Gly His Pro Ser Ser Ala Ala Ser
 165 170 175

Protein Complexes associated with APP-processing
 Ala Pro Val Ser Cys Ser Gly Pro Pro Pro Pro Pro Pro Val
 180 185 190

Pro Pro Pro Pro Thr Gly Ala Thr Pro Pro Pro Pro Pro Pro Leu Pro
 195 200 205

Ala Gly Gly Ala Gln Gly Ser Ser His Asp Glu Ser Ser Met Ser Gly
 210 215 220

Leu Ala Ala Ala Ile Ala Gly Ala Lys Leu Arg Arg Val Gln Arg Pro
 225 230 235 240

Glu Asp Ala Ser Gly Gly Ser Ser Pro Ser Gly Thr Ser Lys Ser Asp
 245 250 255

Ala Asn Arg Ala Ser Ser Gly Gly Gly Gly Gly Gly Leu Met Glu Glu
 260 265 270

Met Asn Lys Leu Leu Ala Lys Arg Arg Lys Ala Ala Ser Gln Ser Asp
 275 280 285

Lys Pro Ala Glu Lys Lys Glu Asp Glu Ser Gln Met Glu Asp Pro Ser
 290 295 300

Thr Ser Pro Ser Pro Gly Thr Arg Ala Ala Ser Gln Pro Pro Asn Ser
 305 310 315 320

Ser Glu Ala Gly Arg Lys Pro Trp Glu Arg Ser Asn Ser Val Glu Lys
 325 330 335

Pro Val Ser Ser Ile Leu Ser Arg Thr Pro Ser Val Ala Lys Ser Pro
 340 345 350

Glu Ala Lys Ser Pro Leu Gln Ser Gln Pro His Ser Arg Met Lys Pro
 355 360 365

Ala Gly Ser Val Asn Asp Met Ala Leu Asp Ala Phe Asp Leu Asp Arg
 370 375 380

Met Lys Gln Glu Ile Leu Glu Glu Val Val Arg Glu Leu His Lys Val
 385 390 395 400

Lys Glu Glu Ile Ile Asp Ala Ile Arg Gln Glu Leu Ser Gly Ile Ser
 405 410 415

Thr Thr

<210> 41

<211> 464

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 41

Met Asp Phe Gln His Arg Pro Gly Gly Lys Thr Gly Ser Gly Gly Val
 1 5 10 15

Ala Ser Ser Ser Glu Ser Asn Arg Asp Arg Arg Glu Arg Leu Arg Gln
 20 25 30

Leu Ala Leu Glu Thr Ile Asp Ile Asn Lys Asp Pro Tyr Phe Met Lys
 35 40 45

Asn His Leu Gly Ser Tyr Glu Cys Lys Leu Cys Leu Thr Leu His Asn
 50 55 60

Asn Glu Gly Ser Tyr Leu Ala His Thr Gln Gly Lys Lys His Gln Thr
 65 70 75 80

Asn Leu Ala Arg Arg Ala Ala Lys Glu Ala Lys Glu Ala Pro Ala Gln
 85 90 95

Pro Ala Pro Glu Lys Val Lys Val Glu Val Lys Lys Phe Val Lys Ile
 100 105 110

Gly Arg Pro Gly Tyr Lys Val Thr Lys Gln Arg Asp Ser Glu Met Gly
 115 120 125

Gln Gln Ser Leu Leu Phe Gln Ile Asp Tyr Pro Glu Ile Ala Glu Gly
 130 135 140

Ile Met Pro Arg His Arg Phe Met Ser Ala Tyr Glu Gln Arg Ile Glu
 145 150 155 160

Pro Pro Asp Arg Arg Trp Gln Tyr Leu Leu Met Ala Ala Glu Pro Tyr
 165 170 175

Glu Thr Ile Ala Phe Lys Val Pro Ser Arg Glu Ile Asp Lys Ala Glu
 180 185 190

Gly Lys Phe Trp Thr His Trp Asn Arg Glu Thr Lys Gln Phe Phe Leu
 195 200 205

Gln Phe His Phe Lys Met Glu Lys Pro Pro Ala Pro Pro Ser Leu Pro
 210 215 220

Ala Gly Pro Pro Gly Val Lys Arg Pro Pro Pro Pro Leu Met Asn Gly
 225 230 235 240

Protein Complexes associated with APP-processing
 Leu Pro Pro Arg Pro Pro Leu Pro Glu Ser Leu Pro Pro Pro Pro Pro
 245 250 255

Gly Gly Leu Pro Leu Pro Pro Met Pro Pro Thr Gly Pro Ala Pro Ser
 260 265 270

Gly Pro Pro Gly Pro Pro Gln Leu Pro Pro Pro Ala Pro Gly Val His
 275 280 285

Pro Pro Ala Pro Val Val His Pro Pro Ala Ser Gly Val His Pro Pro
 290 295 300

Ala Pro Gly Val His Pro Pro Ala Pro Gly Val His Pro Pro Ala Pro
 305 310 315 320

Gly Val His Pro Pro Thr Ser Gly Val His Pro Pro Ala Pro Gly Val
 325 330 335

His Pro Pro Ala Pro Gly Val His Pro Pro Ala Pro Gly Val His Pro
 340 345 350

Pro Ala Pro Gly Val His Pro Pro Ala Pro Gly Val His Pro Pro Pro
 355 360 365

Ser Ala Gly Val His Pro Gln Ala Pro Gly Val His Pro Ala Ala Pro
 370 375 380

Ala Val His Pro Gln Ala Pro Gly Val His Pro Pro Ala Pro Gly Met
 385 390 395 400

His Pro Gln Ala Pro Gly Val His Pro Gln Pro Pro Gly Val His Pro
 405 410 415

Ser Ala Pro Gly Val His Pro Gln Pro Pro Gly Val His Pro Ser Asn
 420 425 430

Pro Gly Val His Pro Pro Thr Pro Met Pro Pro Met Leu Arg Pro Pro
 435 440 445

Leu Pro Ser Glu Gly Pro Gly Asn Ile Pro Pro Pro Pro Pro Thr Asn
 450 455 460

<210> 42

<211> 502

<212> PRT

<213> Homo sapiens

<400> 42

Protein Complexes associated with APP-processing

Met Ala Trp Ala Leu Lys Leu Pro Leu Ala Asp Glu Val Ile Glu Ser
 1 5 10 15

Gly Leu Val Gln Asp Phe Asp Ala Ser Leu Ser Gly Ile Gly Gln Glu
 20 25 30

Leu Gly Ala Gly Ala Tyr Ser Met Ser Asp Val Leu Ala Leu Pro Ile
 35 40 45

Phe Lys Gln Glu Glu Ser Ser Leu Pro Pro Asp Asn Glu Asn Lys Ile
 50 55 60

Leu Pro Phe Gln Tyr Val Leu Cys Ala Ala Thr Ser Pro Ala Val Lys
 65 70 75 80

Leu His Asp Glu Thr Leu Thr Tyr Leu Asn Gln Gly Gln Ser Tyr Glu
 85 90 95

Ile Arg Met Leu Asp Asn Arg Lys Leu Gly Glu Leu Pro Glu Ile Asn
 100 105 110

Gly Lys Leu Val Lys Ser Ile Phe Arg Val Val Phe His Asp Arg Arg
 115 120 125

Leu Gln Tyr Thr Glu His Gln Gln Leu Glu Gly Trp Arg Trp Asn Arg
 130 135 140

Pro Gly Asp Arg Ile Leu Asp Ile Asp Ile Pro Met Ser Val Gly Ile
 145 150 155 160

Ile Asp Pro Arg Ala Asn Pro Thr Gln Leu Asn Thr Val Glu Phe Leu
 165 170 175

Trp Asp Pro Ala Lys Arg Thr Ser Val Phe Ile Gln Val His Cys Ile
 180 185 190

Ser Thr Glu Phe Thr Met Arg Lys His Gly Gly Glu Lys Gly Val Pro
 195 200 205

Phe Arg Val Gln Ile Asp Thr Phe Lys Glu Asn Glu Asn Gly Glu Tyr
 210 215 220

Thr Glu His Leu His Ser Ala Ser Cys Gln Ile Lys Val Phe Lys Pro
 225 230 235 240

Lys Gly Ala Asp Arg Lys Gln Lys Thr Asp Arg Glu Lys Met Glu Lys
 245 250 255

Arg Thr Pro His Glu Lys Glu Lys Tyr Gln Pro Ser Tyr Glu Thr Thr
 260 265 270

Protein Complexes associated with APP-processing

Ile Leu Thr Glu Cys Ser Pro Trp Pro Glu Ile Thr Tyr Val Asn Asn
 275 280 285

Ser Pro Ser Pro Gly Phe Asn Ser Ser His Ser Ser Phe Ser Leu Gly
 290 295 300

Glu Gly Asn Gly Ser Pro Asn His Gln Pro Glu Pro Pro Pro Pro Val
 305 310 315 320

Thr Asp Asn Leu Leu Pro Thr Thr Thr Pro Gln Glu Ala Gln Gln Trp
 325 330 335

Leu His Arg Asn Arg Phe Ser Thr Phe Thr Arg Leu Phe Thr Asn Phe
 340 345 350

Ser Gly Ala Asp Leu Leu Lys Leu Thr Arg Asp Asp Val Ile Gln Ile
 355 360 365

Cys Gly Pro Ala Asp Gly Ile Arg Leu Phe Asn Ala Leu Lys Gly Arg
 370 375 380

Met Val Arg Pro Arg Leu Thr Ile Tyr Val Cys Gln Glu Ser Leu Gln
 385 390 395 400

Leu Arg Glu Gln Gln Gln Gln Gln Gln Gln Gln Lys His Glu
 405 410 415

Asp Gly Asp Ser Asn Gly Thr Phe Phe Val Tyr His Ala Ile Tyr Leu
 420 425 430

Glu Glu Leu Thr Ala Val Glu Leu Thr Glu Lys Ile Ala Gln Leu Phe
 435 440 445

Ser Ile Ser Pro Cys Gln Ile Ser Gln Ile Tyr Lys Gln Gly Pro Thr
 450 455 460

Gly Ile His Val Leu Ile Ser Asp Glu Met Ile Gln Asn Phe Gln Glu
 465 470 475 480

Glu Ala Cys Phe Ile Leu Asp Thr Met Lys Ala Glu Thr Asn Asp Ser
 485 490 495

Tyr His Ile Ile Leu Lys
 500

<210> 43

<211> 438

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 43

Met Gln Glu Asp Arg Asp Gly Ser Cys Ser Thr Val Gly Gly Val Gly
 1 5 10 15
 Tyr Gly Asp Ser Lys Asp Cys Ile Leu Glu Pro Leu Ser Leu Pro Glu
 20 25 30
 Ser Pro Gly Gly Thr Thr Thr Leu Glu Gly Ser Pro Ser Val Pro Cys
 35 40 45
 Ile Phe Cys Glu Glu His Phe Pro Val Ala Glu Gln Asp Lys Leu Leu
 50 55 60
 Lys His Met Ile Ile Glu His Lys Ile Val Ile Ala Asp Val Lys Leu
 65 70 75 80
 Val Ala Asp Phe Gln Arg Tyr Ile Leu Tyr Trp Arg Lys Arg Phe Thr
 85 90 95
 Glu Gln Pro Ile Thr Asp Phe Cys Ser Val Ile Arg Ile Asn Ser Thr
 100 105 110
 Ala Pro Phe Glu Glu Gln Glu Asn Tyr Phe Leu Leu Cys Asp Val Leu
 115 120 125
 Pro Glu Asp Arg Ile Leu Arg Glu Glu Leu Gln Lys Gln Arg Leu Arg
 130 135 140
 Glu Ile Leu Glu Gln Gln Gln Gln Glu Arg Asn Asp Thr Asn Phe His
 145 150 155 160
 Gly Val Cys Met Phe Cys Asn Glu Glu Phe Leu Gly Asn Arg Ser Val
 165 170 175
 Ile Leu Asn His Met Ala Arg Glu His Ala Phe Asn Ile Gly Leu Pro
 180 185 190
 Asp Asn Ile Val Asn Cys Asn Glu Phe Leu Cys Thr Leu Gln Lys Lys
 195 200 205
 Leu Asp Asn Leu Gln Cys Leu Tyr Cys Glu Lys Thr Phe Arg Asp Lys
 210 215 220
 Asn Thr Leu Lys Asp His Met Arg Lys Lys Gln His Arg Lys Ile Asn
 225 230 235 240
 Pro Lys Asn Arg Glu Tyr Asp Arg Phe Tyr Val Ile Asn Tyr Leu Glu
 245 250 255

Protein Complexes associated with APP-processing

Leu Gly Lys Ser Trp Glu Glu Val Gln Leu Glu Asp Asp Arg Glu Leu
 260 265 270

Leu Asp His Gln Glu Asp Asp Trp Ser Asp Trp Glu Glu His Pro Ala
 275 280 285

Ser Ala Val Cys Leu Phe Cys Glu Lys Gln Ala Glu Thr Ile Glu Lys
 290 295 300

Leu Tyr Val His Met Glu Asp Ala His Glu Phe Asp Leu Leu Lys Ile
 305 310 315 320

Lys Ser Glu Leu Gly Leu Asn Phe Tyr Gln Gln Val Lys Leu Val Asn
 325 330 335

Phe Ile Arg Arg Gln Val His Gln Cys Arg Cys Tyr Gly Cys His Val
 340 345 350

Lys Phe Lys Ser Lys Ala Asp Leu Arg Thr His Met Glu Glu Thr Lys
 355 360 365

His Thr Ser Leu Leu Pro Asp Arg Lys Thr Trp Asp Gln Leu Glu Tyr
 370 375 380

Tyr Phe Pro Thr Tyr Glu Asn Asp Thr Leu Leu Cys Thr Leu Ser Asp
 385 390 395 400

Ser Glu Ser Asp Leu Thr Ala Gln Glu Gln Asn Glu Asn Val Pro Ile
 405 410 415

Ile Ser Glu Asp Thr Ser Lys Leu Tyr Ala Leu Lys Gln Ser Ser Ile
 420 425 430

Leu Asn Gln Leu Leu Leu
 435

<210> 44

<211> 1207

<212> PRT

<213> Homo sapiens

<400> 44

Met Arg Leu Thr His Ile Cys Cys Cys Cys Leu Leu Tyr Gln Leu Gly
 1 5 10 15

Phe Leu Ser Asn Gly Ile Val Ser Glu Leu Gln Phe Ala Pro Asp Arg
 20 25 30

Protein Complexes associated with APP-processing

Glu Glu Trp Glu Val Val Phe Pro Ala Leu Trp Arg Arg Glu Pro Val
 35 40 45

Asp Pro Ala Gly Gly Ser Gly Gly Ser Ala Asp Pro Gly Trp Val Arg
 50 55 60

Gly Val Gly Gly Gly Gly Ser Ala Arg Ala Gln Ala Ala Gly Ser Ser
 65 70 75 80

Arg Glu Val Arg Ser Val Ala Pro Val Pro Leu Glu Glu Pro Val Glu
 85 90 95

Gly Arg Ser Glu Ser Arg Leu Arg Pro Pro Pro Pro Ser Glu Gly Glu
 100 105 110

Glu Asp Glu Glu Leu Glu Ser Gln Glu Leu Pro Arg Gly Ser Ser Gly
 115 120 125

Ala Ala Ala Leu Ser Pro Gly Ala Pro Ala Ser Trp Gln Pro Pro Pro
 130 135 140

Pro Pro Gln Pro Pro Pro Ser Pro Pro Pro Ala Gln His Ala Glu Pro
 145 150 155 160

Asp Gly Asp Glu Val Leu Leu Arg Ile Pro Ala Phe Ser Arg Asp Leu
 165 170 175

Tyr Leu Leu Leu Arg Arg Asp Gly Arg Phe Leu Ala Pro Arg Phe Ala
 180 185 190

Val Glu Gln Arg Pro Asn Pro Gly Pro Gly Pro Thr Gly Ala Ala Ser
 195 200 205

Ala Pro Gln Pro Pro Ala Pro Pro Asp Ala Gly Cys Phe Tyr Thr Gly
 210 215 220

Ala Val Leu Arg His Pro Gly Ser Leu Ala Ser Phe Ser Thr Cys Gly
 225 230 235 240

Gly Gly Leu Met Gly Phe Ile Gln Leu Asn Glu Asp Phe Ile Phe Ile
 245 250 255

Glu Pro Leu Asn Asp Thr Met Ala Ile Thr Gly His Pro His Arg Val
 260 265 270

Tyr Arg Gln Lys Arg Ser Met Glu Glu Lys Val Thr Glu Lys Ser Ala
 275 280 285

Leu His Ser His Tyr Cys Gly Ile Ile Ser Asp Lys Gly Arg Pro Arg
 290 295 300

Protein Complexes associated with APP-processing

Ser Arg Lys Ile Ala Glu Ser Gly Arg Gly Lys Arg Tyr Ser Tyr Lys
 305 310 315 320

Leu Pro Gln Glu Tyr Asn Ile Glu Thr Val Val Val Ala Asp Pro Ala
 325 330 335

Met Val Ser Tyr His Gly Ala Asp Ala Ala Arg Arg Phe Ile Leu Thr
 340 345 350

Ile Leu Asn Met Val Phe Asn Leu Phe Gln His Lys Ser Leu Gly Val
 355 360 365

Gln Val Asn Leu Arg Val Ile Lys Leu Ile Leu Leu His Glu Thr Pro
 370 375 380

Pro Glu Leu Tyr Ile Gly His His Gly Glu Lys Met Leu Glu Ser Phe
 385 390 395 400

Cys Lys Trp Gln His Glu Glu Phe Gly Lys Lys Asn Asp Ile His Leu
 405 410 415

Glu Met Ser Thr Asn Trp Gly Glu Asp Met Thr Ser Val Asp Ala Ala
 420 425 430

Ile Leu Ile Thr Arg Lys Asp Phe Cys Val His Lys Asp Glu Pro Cys
 435 440 445

Asp Thr Val Gly Ile Ala Tyr Leu Ser Gly Met Cys Ser Glu Lys Arg
 450 455 460

Lys Cys Ile Ile Ala Glu Asp Asn Gly Leu Asn Leu Ala Phe Thr Ile
 465 470 475 480

Ala His Glu Met Gly His Asn Met Gly Ile Asn His Asp Asn Asp His
 485 490 495

Pro Ser Cys Ala Asp Gly Leu His Ile Met Ser Gly Glu Trp Ile Lys
 500 505 510

Gly Gln Asn Leu Gly Asp Val Ser Trp Ser Arg Cys Ser Lys Glu Asp
 515 520 525

Leu Glu Arg Phe Leu Arg Ser Lys Ala Ser Asn Cys Leu Leu Gln Thr
 530 535 540

Asn Pro Gln Ser Val Asn Ser Val Met Val Pro Ser Lys Leu Pro Gly
 545 550 555 560

Met Thr Tyr Thr Ala Asp Glu Gln Cys Gln Ile Leu Phe Gly Pro Leu
 565 570 575

Protein Complexes associated with APP-processing

Ala Ser Phe Cys Gln Glu Met Gln His Val Ile Cys Thr Gly Leu Trp
580 585 590

Cys Lys Val Glu Gly Glu Lys Glu Cys Arg Thr Lys Leu Asp Pro Pro
595 600 605

Met Asp Gly Thr Asp Cys Asp Leu Gly Lys Trp Cys Lys Ala Gly Glu
610 615 620

Cys Thr Ser Arg Thr Ser Ala Pro Glu His Leu Ala Gly Glu Trp Ser
625 630 635 640

Leu Trp Ser Pro Cys Ser Arg Thr Cys Ser Ala Gly Ile Ser Ser Arg
645 650 655

Glu Arg Lys Cys Pro Gly Leu Asp Ser Glu Ala Arg Asp Cys Asn Gly
660 665 670

Pro Arg Lys Gln Tyr Arg Ile Cys Glu Asn Pro Pro Cys Pro Ala Gly
675 680 685

Leu Pro Gly Phe Arg Asp Trp Gln Cys Gln Ala Tyr Ser Val Arg Thr
690 695 700

Ser Ser Pro Lys His Ile Leu Gln Trp Gln Ala Val Leu Asp Glu Glu
705 710 715 720

Lys Pro Cys Ala Leu Phe Cys Ser Pro Val Gly Lys Glu Gln Pro Ile
725 730 735

Leu Leu Ser Glu Lys Val Met Asp Gly Thr Ser Cys Gly Tyr Gln Gly
740 745 750

Leu Asp Ile Cys Ala Asn Gly Arg Cys Gln Lys Val Gly Cys Asp Gly
755 760 765

Leu Leu Gly Ser Leu Ala Arg Glu Asp His Cys Gly Val Cys Asn Gly
770 775 780

Asn Gly Lys Ser Cys Lys Ile Ile Lys Gly Asp Phe Asn His Thr Arg
785 790 795 800

Gly Ala Gly Tyr Val Glu Val Leu Val Ile Pro Ala Gly Ala Arg Arg
805 810 815

Ile Lys Val Val Glu Glu Lys Pro Ala His Ser Tyr Leu Ala Leu Arg
820 825 830

Asp Ala Gly Lys Gln Ser Ile Asn Ser Asp Trp Lys Ile Glu His Ser
835 840 845

Protein Complexes associated with APP-processing
 Gly Ala Phe Asn Leu Ala Gly Thr Thr Val His Tyr Val Arg Arg Gly
 850 855 860

Leu Trp Glu Lys Ile Ser Ala Lys Gly Pro Thr Thr Ala Pro Leu His
 865 870 875 880

Leu Leu Val Leu Leu Phe Gln Asp Gln Asn Tyr Gly Leu His Tyr Glu
 885 890 895

Tyr Thr Ile Pro Ser Asp Pro Leu Pro Glu Asn Gln Ser Ser Lys Ala
 900 905 910

Pro Glu Pro Leu Phe Met Trp Thr His Thr Ser Trp Glu Asp Cys Asp
 915 920 925

Ala Thr Cys Gly Gly Gly Glu Arg Lys Thr Thr Val Ser Cys Thr Lys
 930 935 940

Ile Met Ser Lys Asn Ile Ser Ile Val Asp Asn Glu Lys Cys Lys Tyr
 945 950 955 960

Leu Thr Lys Pro Glu Pro Gln Ile Arg Lys Cys Asn Glu Gln Pro Cys
 965 970 975

Gln Thr Arg Trp Met Met Thr Glu Trp Thr Pro Cys Ser Arg Thr Cys
 980 985 990

Gly Lys Gly Met Gln Ser Arg Gln Val Ala Cys Thr Gln Gln Leu Ser
 995 1000 1005

Asn Gly Thr Leu Ile Arg Ala Arg Glu Arg Asp Cys Ile Gly Pro
 1010 1015 1020

Lys Pro Ala Ser Ala Gln Arg Cys Glu Gly Gln Asp Cys Met Thr
 1025 1030 1035

Val Trp Glu Ala Gly Val Trp Ser Glu Phe Ser Val Lys Cys Gly
 1040 1045 1050

Lys Gly Ile Arg His Arg Thr Val Arg Cys Thr Asn Pro Arg Lys
 1055 1060 1065

Lys Cys Val Leu Ser Thr Arg Pro Arg Glu Ala Glu Asp Cys Glu
 1070 1075 1080

Asp Tyr Ser Lys Cys Tyr Val Trp Arg Met Gly Asp Trp Ser Lys
 1085 1090 1095

Cys Ser Ile Thr Cys Gly Lys Gly Met Gln Ser Arg Val Ile Gln
 1100 1105 1110

Protein Complexes associated with APP-processing
 Cys Met His Lys Ile Thr Gly Arg His Gly Asn Glu Cys Phe Ser
 1115 1120 1125

Ser Glu Lys Pro Ala Ala Tyr Arg Pro Cys His Leu Gln Pro Cys
 1130 1135 1140

Asn Glu Lys Ile Asn Val Asn Thr Ile Thr Ser Pro Arg Leu Ala
 1145 1150 1155

Ala Leu Thr Phe Lys Cys Leu Gly Asp Gln Trp Pro Val Tyr Cys
 1160 1165 1170

Arg Val Ile Arg Glu Lys Asn Leu Cys Gln Asp Met Arg Trp Tyr
 1175 1180 1185

Gln Arg Cys Cys Glu Thr Cys Arg Asp Phe Tyr Ala Gln Lys Leu
 1190 1195 1200

Gln Gln Lys Ser
 1205

<210> 45

<211> 4501

<212> PRT

<213> Homo sapiens

<400> 45

Met Met Lys Leu Tyr Ile Asp Asn Ala Ala Pro Asp Lys Leu Lys Gly
 1 5 10 15

Leu Cys Ile Phe Phe Val Arg Cys Arg Asn Asp Val Ala Ile Asn Val
 20 25 30

Lys Thr Ile Gln Glu Glu Ala Leu Phe Thr Val Leu Asp Ala Ser Lys
 35 40 45

Gly Leu Leu Asn Gly Ile Arg Asp Met Leu Ala Asn Ile Phe Leu Pro
 50 55 60

Ala Val Leu Ala Thr Asn Asn Trp Gly Ala Leu Asn Gln Ser Lys Gln
 65 70 75 80

Gly Glu Ser Glu Lys His Ile Phe Thr Glu Thr Ile Asn Arg Tyr Leu
 85 90 95

Ser Phe Leu Asp Gly Ala Arg Ile Ser Ile Glu Gly Thr Val Lys Leu
 100 105 110

Protein Complexes associated with APP-processing

Lys Thr Ile Asp Asn Val Asn Phe Ser Lys Leu His Thr Phe Glu Glu
115 120 125

Val Thr Ala Ala Ala Ser Asn Ser Glu Thr Val His Gln Leu Glu Glu
130 135 140

Val Leu Met Val Trp Tyr Lys Gln Ile Glu Gln Val Leu Ile Glu Ser
145 150 155 160

Glu Gln Met Arg Lys Glu Ala Gly Asp Ser Gly Pro Leu Thr Glu Leu
165 170 175

Glu His Trp Lys Arg Met Ser Ala Lys Phe Asn Tyr Ile Ile Glu Gln
180 185 190

Ile Lys Gly Pro Ser Cys Lys Ala Val Ile Asn Val Leu Asn Val Ala
195 200 205

His Ser Lys Leu Leu Lys Asn Trp Arg Asp Leu Asp Ala Arg Ile Thr
210 215 220

Asp Thr Ala Asn Glu Ser Lys Asp Asn Val Arg Tyr Leu Tyr Thr Leu
225 230 235 240

Glu Lys Val Cys Gln Pro Leu Tyr Asn His Asp Leu Val Ser Met Ala
245 250 255

His Gly Ile Gln Asn Leu Ile Asn Ala Ile Arg Met Ile His Gly Val
260 265 270

Ser Arg Tyr Tyr Asn Thr Ser Glu Arg Met Thr Ser Leu Phe Ile Lys
275 280 285

Val Thr Asn Gln Met Val Thr Ala Cys Lys Ala Tyr Ile Thr Asp Gly
290 295 300

Gly Leu Asn His Val Trp Asp Gln Glu Thr Pro Val Val Leu Lys Lys
305 310 315 320

Ile Gln Asp Cys Ile Phe Leu Phe Lys Glu Tyr Gln Ala Ser Phe His
325 330 335

Lys Thr Arg Lys Leu Ile Ser Glu Ser Ser Gly Glu Lys Ser Phe Glu
340 345 350

Val Ser Glu Met Tyr Ile Phe Gly Lys Phe Glu Ala Phe Cys Lys Arg
355 360 365

Leu Glu Lys Ile Thr Glu Met Ile Thr Val Val Gln Thr Tyr Ser Thr
370 375 380

Protein Complexes associated with APP-processing

Leu Ser Asn Ser Thr Ile Glu Gly Ile Asp Ile Met Ala Ile Lys Phe
 385 390 395 400

Arg Asn Ile Tyr Gln Gly Val Lys Lys Lys Gln Tyr Asp Ile Leu Asp
 405 410 415

Pro Arg Arg Thr Glu Phe Asp Thr Asp Phe Leu Asp Phe Met Thr Lys
 420 425 430

Ile Asn Gly Leu Glu Val Gln Ile Gln Ala Phe Met Asn Ser Ser Phe
 435 440 445

Gly Lys Ile Leu Ser Ser Gln Gln Ala Leu Gln Leu Leu Gln Arg Phe
 450 455 460

Gln Lys Leu Asn Ile Pro Cys Leu Gly Leu Glu Ile Asn His Thr Ile
 465 470 475 480

Glu Arg Ile Leu Gln Tyr Tyr Val Ala Glu Leu Asp Ala Thr Lys Lys
 485 490 495

Ala Ser Leu Tyr His Ser Gln Lys Asp Asp Pro Pro Leu Ala Arg Asn
 500 505 510

Met Pro Pro Ile Ala Gly Lys Ile Leu Trp Val Arg Gln Leu Tyr Arg
 515 520 525

Arg Ile Ser Glu Pro Ile Asn Tyr Phe Phe Lys Asn Ser Asp Ile Leu
 530 535 540

Ser Ser Pro Asp Gly Lys Ala Val Ile Arg Gln Tyr Asn Lys Ile Ser
 545 550 555 560

Tyr Val Leu Val Glu Phe Glu Val Val Tyr His Thr Ala Trp Ile Arg
 565 570 575

Glu Ile Ser Gln Leu His Tyr Ala Leu Gln Ala Thr Leu Phe Val Arg
 580 585 590

His Pro Glu Thr Gly Lys Leu Leu Val Asn Phe Asp Pro Lys Ile Leu
 595 600 605

Glu Val Val Arg Glu Thr Lys Cys Met Ile Lys Met Lys Leu Asp Val
 610 615 620

Pro Glu Gln Ala Lys Arg Leu Leu Lys Leu Glu Ser Lys Leu Lys Ala
 625 630 635 640

Asp Lys Leu Tyr Leu Gln Gly Leu Leu Gln Tyr Tyr Asp Glu Leu Cys
 645 650 655

Protein Complexes associated with APP-processing

Gln Glu Val Pro Ser Val Phe Val Asn Leu Met Thr Pro Lys Met Lys
660 665 670

Lys Val Glu Ser Val Leu Arg Gln Gly Leu Thr Val Leu Thr Trp Ser
675 680 685

Ser Leu Thr Leu Glu Ser Phe Phe Gln Glu Val Glu Leu Val Leu Asp
690 695 700

Met Phe Asn Gln Leu Leu Lys Lys Ile Ser Asp Leu Cys Glu Met His
705 710 715 720

Ile Asp Thr Val Leu Lys Glu Ile Ala Lys Thr Val Leu Ile Ser Leu
725 730 735

Pro Glu Ser Gly Ala Thr Lys Val Glu Asp Met Leu Thr Leu Asn Glu
740 745 750

Thr Tyr Thr Lys Glu Trp Ala Asp Ile Leu Asn His Lys Ser Lys His
755 760 765

Val Glu Glu Ala Val Arg Glu Leu Ile Ser Ile Phe Glu Gln Ile Tyr
770 775 780

Glu Val Lys Tyr Thr Gly Lys Val Gly Lys Gln Ser Glu Gln Arg Lys
785 790 795 800

His Val Val Phe Gly Ser Glu Thr Gly Glu Gly Glu Asn Asn Asp Tyr
805 810 815

Glu Ala Asn Ile Val Asn Glu Phe Asp Thr His Asp Lys Glu Asp Glu
820 825 830

Phe Lys Lys Glu Cys Lys Glu Val Phe Ala Phe Phe Ser His Gln Leu
835 840 845

Leu Asp Ser Leu Gln Lys Ala Thr Arg Leu Ser Leu Asp Thr Met Lys
850 855 860

Arg Arg Ile Phe Val Ala Arg Gln Val Glu Asn Met Leu Ile Ile Leu
865 870 875 880

Tyr Gly Arg Lys Gln Ser Glu Asp Ile Ile Ser Phe Ile Lys Ser Glu
885 890 895

Val His Leu Ala Ile Pro Asn Val Val Met Ile Pro Ser Leu Asp Asp
900 905 910

Ile Gln Gln Ala Ile Asn Arg Met Ile Gln Leu Thr Leu Glu Val Ser
915 920 925

Protein Complexes associated with APP-processing
 Arg Gly Val Ala His Trp Gly Gln Gln Gln Ile Arg Pro Ile Lys Ser
 930 935 940

Val Ile Pro Ser Pro Thr Thr Thr Asp Val Thr His Gln Asn Thr Gly
 945 950 955 960

Lys Leu Leu Lys Lys Glu Glu Arg Ser Phe Glu Glu Ala Ile Pro Ala
 965 970 975

Arg Lys Leu Lys Asn Phe Tyr Pro Gly Val Ala Glu His Lys Asp Ile
 980 985 990

Ser Lys Leu Val Leu Leu Leu Ser Ser Ser Val Asn Ser Leu Arg Lys
 995 1000 1005

Ala Ala His Glu Ala Leu Gln Asp Phe Gln Lys Tyr Lys Thr Leu
 1010 1015 1020

Trp Thr Glu Asp Arg Asp Val Lys Val Lys Glu Phe Leu Ala Asn
 1025 1030 1035

Asn Pro Ser Leu Thr Glu Ile Arg Ser Glu Ile Leu His Tyr Ala
 1040 1045 1050

Thr Phe Glu Gln Glu Ile Asp Glu Leu Lys Pro Ile Ile Val Val
 1055 1060 1065

Gly Ala Leu Glu Leu His Thr Glu Pro Met Lys Leu Ala Leu Ser
 1070 1075 1080

Ile Glu Ala Lys Ala Trp Lys Met Leu Leu Cys Arg Tyr Leu Asn
 1085 1090 1095

Glu Glu Tyr Lys Lys Lys Met Ser Tyr Met Ile Ala Phe Ile Asn
 1100 1105 1110

Glu Tyr Leu Lys Lys Leu Ser Arg Pro Ile Arg Asp Leu Asp Asp
 1115 1120 1125

Val Arg Phe Ala Met Glu Ala Leu Ser Cys Ile Arg Asp Asn Glu
 1130 1135 1140

Ile Gln Met Asp Met Thr Leu Gly Pro Ile Glu Glu Ala Tyr Ala
 1145 1150 1155

Ile Leu Asn Arg Phe Glu Val Glu Val Thr Lys Glu Glu Ser Glu
 1160 1165 1170

Ala Val Asp Thr Leu Arg Tyr Ser Phe Asn Lys Leu Gln Ser Lys
 1175 1180 1185

Protein Complexes associated with APP-processing

Ala Val	Ser Val	Gln Glu	Asp	Leu Val	Gln Val	Gln	Pro Lys Phe
1190			1195			1200	
Lys Ser	Asn Leu	Leu Glu	Ser	Val Glu	Val Phe	Arg	Glu Asp Val
1205			1210			1215	
Ile Asn	Phe Ala	Glu Ala	Tyr	Glu Leu	Glu Gly	Pro	Met Val Pro
1220			1225			1230	
Asn Ile	Pro Pro	Gln Glu	Ala	Ser Asn	Arg Leu	Gln	Ile Phe Gln
1235			1240			1245	
Ala Ser	Phe Asp	Asp Leu	Trp	Arg Lys	Phe Val	Thr	Tyr Ser Ser
1250			1255			1260	
Gly Glu	Gln Leu	Phe Gly	Leu	Pro Val	Thr Asp	Tyr	Glu Val Leu
1265			1270			1275	
His Lys	Thr Arg	Lys Glu	Leu	Asn Leu	Leu Gln	Lys	Leu Tyr Gly
1280			1285			1290	
Leu Tyr	Asp Thr	Val Met	Ser	Ser Ile	Ser Gly	Tyr	Tyr Glu Ile
1295			1300			1305	
Leu Trp	Gly Asp	Val Asp	Ile	Glu Lys	Ile Asn	Ala	Glu Leu Leu
1310			1315			1320	
Glu Phe	Gln Asn	Arg Cys	Arg	Lys Leu	Pro Lys	Gly	Leu Lys Asp
1325			1330			1335	
Trp Gln	Ala Phe	Leu Asp	Leu	Lys Lys	Arg Ile	Asp	Asp Phe Ser
1340			1345			1350	
Glu Ser	Cys Pro	Leu Leu	Glu	Met Met	Thr Asn	Lys	Ala Met Lys
1355			1360			1365	
Gln Arg	His Trp	Asp Arg	Ile	Ser Glu	Leu Thr	Gly	Thr Pro Phe
1370			1375			1380	
Asp Val	Glu Ser	Asp Ser	Phe	Cys Leu	Arg Asn	Ile	Met Glu Ala
1385			1390			1395	
Pro Leu	Leu Lys	His Lys	Asp	Asp Ile	Glu Asp	Ile	Cys Ile Ser
1400			1405			1410	
Ala Ile	Lys Glu	Lys Asp	Ile	Glu Ala	Lys Leu	Thr	Gln Val Ile
1415			1420			1425	
Glu Asn	Trp Thr	Asn Gln	Asn	Leu Ser	Phe Ala	Ala	Phe Lys Gly
1430			1435			1440	

Protein Complexes associated with APP-processing

Lys Gly Glu Leu Leu Leu Lys Gly Thr Glu Ser Gly Glu Ile Ile
1445 1450 1455

Thr Leu Met Glu Asp Ser Leu Met Val Leu Gly Ser Leu Leu Ser
1460 1465 1470

Asn Arg Tyr Asn Ala Pro Phe Lys Lys Asn Ile Gln Asn Trp Val
1475 1480 1485

Tyr Lys Leu Ser Thr Ser Ser Asp Ile Ile Glu Glu Trp Leu Val
1490 1495 1500

Val Gln Asn Leu Trp Val Tyr Leu Glu Ala Val Phe Val Gly Gly
1505 1510 1515

Asp Ile Ala Lys Gln Leu Pro Gln Glu Ala Lys Arg Phe Gln Asn
1520 1525 1530

Ile Asp Lys Ser Trp Ile Lys Ile Met Gln Arg Ala His Glu Asn
1535 1540 1545

Pro Asn Val Ile Asn Cys Cys Val Gly Asp Glu Thr Met Gly Gln
1550 1555 1560

Leu Leu Pro His Leu His Glu Gln Leu Glu Val Cys Gln Lys Ser
1565 1570 1575

Leu Thr Gly Tyr Leu Glu Lys Lys Arg Leu Leu Phe Pro Arg Phe
1580 1585 1590

Phe Phe Val Ser Asp Pro Val Leu Leu Glu Ile Leu Gly Gln Ala
1595 1600 1605

Ser Asp Ser His Thr Ile Gln Pro His Leu Pro Ala Val Ser Asp
1610 1615 1620

Asn Ile Asn Glu Val Thr Phe His Ala Lys Asp Tyr Asp Arg Ile
1625 1630 1635

Met Ala Val Ile Ser Arg Glu Gly Glu Lys Ile Val Leu Asp Asn
1640 1645 1650

Ser Val Met Ala Lys Gly Pro Val Glu Ile Trp Leu Leu Asp Leu
1655 1660 1665

Leu Lys Met Gln Met Ser Ser Leu His Asn Ile Ile Arg Ser Ala
1670 1675 1680

Phe Tyr Gln Ile Ser Asp Ser Gly Phe Gln Leu Leu Pro Phe Leu
1685 1690 1695

Protein Complexes associated with APP-processing

Ser	His	Phe	Pro	Ala	Gln	Val	Gly	Leu	Leu	Gly	Ile	Gln	Met	Leu
1700						1705					1710			
Trp	Thr	His	Asp	Ser	Glu	Glu	Ala	Leu	Arg	Asn	Ala	Lys	Asp	Asp
1715						1720					1725			
Arg	Lys	Ile	Met	Gln	Val	Thr	Asn	Gln	Lys	Phe	Leu	Asp	Ile	Leu
1730						1735					1740			
Asn	Thr	Leu	Ile	Ser	Gln	Thr	Thr	His	Asp	Leu	Ser	Lys	Phe	Asp
1745						1750					1755			
Arg	Val	Lys	Phe	Glu	Thr	Leu	Ile	Thr	Ile	His	Val	His	Gln	Arg
1760						1765					1770			
Asp	Ile	Phe	Asp	Asp	Leu	Val	Lys	Met	His	Ile	Lys	Ser	Pro	Thr
1775						1780					1785			
Asp	Phe	Glu	Trp	Leu	Lys	Gln	Ser	Arg	Phe	Tyr	Phe	Lys	Glu	Asp
1790						1795					1800			
Leu	Asp	Gln	Thr	Val	Val	Ser	Ile	Thr	Asp	Val	Asp	Phe	Ile	Tyr
1805						1810					1815			
Gln	Asn	Glu	Phe	Leu	Gly	Cys	Thr	Asp	Arg	Leu	Val	Ile	Thr	Pro
1820						1825					1830			
Leu	Thr	Asp	Arg	Cys	Tyr	Ile	Thr	Leu	Ala	Gln	Ala	Leu	Gly	Met
1835						1840					1845			
Asn	Met	Gly	Gly	Ala	Pro	Ala	Gly	Pro	Ala	Gly	Thr	Gly	Lys	Thr
1850						1855					1860			
Glu	Thr	Thr	Lys	Asp	Met	Gly	Arg	Cys	Leu	Gly	Lys	Tyr	Val	Val
1865						1870					1875			
Val	Phe	Asn	Cys	Ser	Asp	Gln	Met	Asp	Phe	Arg	Gly	Leu	Gly	Arg
1880						1885					1890			
Ile	Phe	Lys	Gly	Lys	Cys	Leu	Ala	Gln	Ser	Gly	Ser	Trp	Gly	Cys
1895						1900					1905			
Phe	Asp	Glu	Phe	Asn	Arg	Ile	Glu	Leu	Pro	Val	Leu	Ser	Val	Ala
1910						1915					1920			
Ala	Gln	Gln	Ile	Tyr	Ile	Val	Leu	Thr	Ala	Arg	Lys	Glu	Arg	Lys
1925						1930					1935			
Lys	Gln	Phe	Ile	Phe	Ser	Asp	Gly	Asp	Cys	Val	Asp	Leu	Asn	Pro
1940						1945					1950			

Protein Complexes associated with APP-processing

Glu	Phe	Gly	Ile	Phe	Leu	Thr	Met	Asn	Pro	Gly	Tyr	Ala	Gly	Arg
	1955					1960					1965			
Gln	Glu	Leu	Pro	Glu	Asn	Lys	Ile	Gln	Phe	Arg	Thr	Val	Ala	Met
	1970					1975					1980			
Met	Val	Pro	Asp	Arg	Gln	Ile	Ile	Met	Arg	Val	Lys	Leu	Ala	Ser
	1985					1990					1995			
Cys	Gly	Phe	Leu	Glu	Asn	Val	Ile	Leu	Ala	Gln	Lys	Phe	Tyr	Val
	2000					2005					2010			
Leu	Tyr	Lys	Leu	Cys	Glu	Glu	Gln	Leu	Thr	Lys	Gln	Val	His	Tyr
	2015					2020					2025			
Asp	Phe	Gly	Leu	Arg	Asn	Ile	Leu	Ser	Val	Leu	Arg	Thr	Leu	Gly
	2030					2035					2040			
Ser	Gln	Lys	Arg	Ala	Arg	Pro	Glu	Asp	Ser	Glu	Leu	Ser	Ile	Val
	2045					2050					2055			
Met	Arg	Gly	Leu	Arg	Asp	Met	Asn	Leu	Ser	Lys	Leu	Val	Asp	Glu
	2060					2065					2070			
Asp	Glu	Pro	Leu	Phe	Leu	Ser	Leu	Ile	Asn	Asp	Leu	Phe	Pro	Gly
	2075					2080					2085			
Leu	Gln	Leu	Asp	Ser	Asn	Thr	Tyr	Ala	Glu	Leu	Gln	Asn	Ala	Val
	2090					2095					2100			
Ala	His	Gln	Val	Gln	Ile	Glu	Gly	Leu	Ile	Asn	His	Pro	Pro	Trp
	2105					2110					2115			
Asn	Leu	Lys	Leu	Val	Gln	Leu	Tyr	Glu	Thr	Ser	Leu	Val	Arg	His
	2120					2125					2130			
Gly	Leu	Met	Thr	Leu	Gly	Pro	Ser	Gly	Ser	Gly	Lys	Thr	Thr	Val
	2135					2140					2145			
Ile	Thr	Ile	Leu	Met	Lys	Ala	Gln	Thr	Glu	Cys	Gly	Arg	Pro	His
	2150					2155					2160			
Arg	Glu	Met	Arg	Met	Asn	Pro	Lys	Ala	Ile	Thr	Ala	Pro	Gln	Met
	2165					2170					2175			
Phe	Gly	Arg	Leu	Asp	Thr	Ala	Thr	Asn	Asp	Trp	Thr	Asp	Gly	Ile
	2180					2185					2190			
Phe	Ser	Thr	Leu	Trp	Arg	Lys	Thr	Leu	Lys	Ala	Lys	Lys	Gly	Glu
	2195					2200					2205			

Protein Complexes associated with APP-processing

Asn Ile Phe Leu Ile Leu Asp Gly Pro Val Asp Ala Ile Trp Ile
 2210 2215 2220

Glu Asn Leu Asn Ser Val Leu Asp Asp Asn Lys Thr Leu Thr Leu
 2225 2230 2235

Ala Asn Gly Asp Arg Ile Pro Met Ala Pro Ser Cys Lys Leu Leu
 2240 2245 2250

Phe Glu Val His Asn Ile Glu Asn Ala Ser Pro Ala Thr Val Ser
 2255 2260 2265

Arg Met Gly Met Val Tyr Ile Ser Ser Ser Ala Leu Ser Trp Arg
 2270 2275 2280

Pro Ile Leu Gln Ala Trp Leu Lys Lys Arg Thr Ala Gln Glu Ala
 2285 2290 2295

Ala Val Phe Leu Thr Leu Tyr Glu Lys Val Phe Glu Asp Thr Tyr
 2300 2305 2310

Thr Tyr Met Lys Leu Asn Leu Asn Pro Lys Met Gln Leu Leu Glu
 2315 2320 2325

Cys Asn Tyr Ile Val Gln Ser Leu Asn Leu Leu Glu Gly Leu Ile
 2330 2335 2340

Pro Ser Lys Glu Glu Gly Gly Val Ser Cys Val Glu His Leu His
 2345 2350 2355

Lys Leu Phe Val Phe Gly Leu Met Trp Ser Leu Gly Ala Leu Leu
 2360 2365 2370

Glu Leu Glu Ser Arg Glu Lys Leu Glu Ala Phe Leu Arg Gln His
 2375 2380 2385

Glu Ser Lys Leu Asp Leu Pro Glu Ile Pro Lys Gly Ser Asn Gln
 2390 2395 2400

Thr Met Tyr Glu Phe Tyr Val Thr Asp Tyr Gly Asp Trp Glu His
 2405 2410 2415

Trp Asn Lys Lys Leu Gln Pro Tyr Tyr Tyr Pro Thr Asp Ser Ile
 2420 2425 2430

Pro Glu Tyr Ser Ser Ile Leu Val Pro Asn Val Asp Asn Ile Arg
 2435 2440 2445

Thr Asn Phe Leu Ile Asp Thr Ile Ala Lys Gln His Lys Ala Val
 2450 2455 2460

Protein Complexes associated with APP-processing

Leu	Leu	Thr	Gly	Glu	Gln	Gly	Thr	Ala	Lys	Thr	Val	Met	Val	Lys
	2465					2470					2475			
Ala	Tyr	Leu	Lys	Lys	Tyr	Asp	Pro	Glu	Val	Gln	Leu	Ser	Lys	Ser
	2480					2485					2490			
Leu	Asn	Phe	Ser	Ser	Ala	Thr	Glu	Pro	Met	Met	Phe	Gln	Arg	Thr
	2495					2500					2505			
Ile	Glu	Ser	Tyr	Val	Asp	Lys	Arg	Ile	Gly	Ser	Thr	Tyr	Gly	Pro
	2510					2515					2520			
Pro	Gly	Gly	Arg	Lys	Met	Thr	Val	Phe	Ile	Asp	Asp	Ile	Asn	Met
	2525					2530					2535			
Pro	Val	Ile	Asn	Glu	Trp	Gly	Asp	Gln	Ile	Thr	Asn	Glu	Ile	Val
	2540					2545					2550			
Arg	Gln	Met	Met	Glu	Met	Glu	Gly	Met	Tyr	Ser	Leu	Asp	Lys	Pro
	2555					2560					2565			
Gly	Asp	Phe	Thr	Thr	Ile	Val	Asp	Val	Gln	Leu	Ile	Ala	Ala	Met
	2570					2575					2580			
Ile	His	Pro	Gly	Gly	Gly	Arg	Asn	Asp	Ile	Pro	Gln	Arg	Leu	Lys
	2585					2590					2595			
Arg	Gln	Phe	Thr	Val	Phe	Asn	Cys	Thr	Leu	Pro	Ser	Asn	Ala	Ser
	2600					2605					2610			
Ile	Asp	Lys	Ile	Phe	Gly	Ile	Ile	Gly	Cys	Gly	Tyr	Phe	Asp	Pro
	2615					2620					2625			
Cys	Arg	Ser	Phe	Lys	Pro	Gln	Ile	Cys	Glu	Met	Ile	Val	Asn	Leu
	2630					2635					2640			
Val	Ser	Val	Gly	Arg	Val	Leu	Trp	Gln	Trp	Thr	Lys	Val	Lys	Met
	2645					2650					2655			
Leu	Pro	Thr	Pro	Ser	Lys	Phe	His	Tyr	Ile	Phe	Asn	Leu	Arg	Asp
	2660					2665					2670			
Leu	Ser	Arg	Ile	Trp	Gln	Gly	Met	Leu	Thr	Ile	Lys	Ala	Glu	Glu
	2675					2680					2685			
Cys	Ala	Ser	Ile	Pro	Thr	Leu	Leu	Ser	Leu	Phe	Lys	His	Glu	Cys
	2690					2695					2700			
Ser	Arg	Val	Ile	Ala	Asp	Arg	Phe	Ile	Thr	Pro	Glu	Asp	Glu	Gln
	2705					2710					2715			

Protein Complexes associated with APP-processing

Trp	Phe	Asn	Ala	His	Leu	Thr	Arg	Ala	Val	Glu	Glu	Asn	Ile	Gly
	2720					2725					2730			
Ser	Asp	Ala	Ala	Ser	Cys	Ile	Leu	Pro	Glu	Pro	Tyr	Phe	Val	Asp
	2735					2740					2745			
Phe	Leu	Arg	Glu	Met	Pro	Glu	Pro	Thr	Gly	Asp	Glu	Pro	Glu	Asp
	2750					2755					2760			
Ser	Val	Phe	Glu	Val	Pro	Lys	Ile	Tyr	Glu	Leu	Met	Pro	Ser	Phe
	2765					2770					2775			
Asp	Phe	Leu	Ala	Glu	Lys	Leu	Gln	Phe	Tyr	Gln	Arg	Gln	Phe	Asn
	2780					2785					2790			
Glu	Ile	Ile	Arg	Gly	Thr	Ser	Leu	Asp	Leu	Val	Phe	Phe	Lys	Asp
	2795					2800					2805			
Ala	Met	Thr	His	Leu	Ile	Lys	Ile	Ser	Arg	Ile	Ile	Arg	Thr	Ser
	2810					2815					2820			
Cys	Gly	Asn	Ala	Leu	Leu	Val	Gly	Val	Gly	Gly	Ser	Gly	Lys	Gln
	2825					2830					2835			
Ser	Leu	Ser	Arg	Leu	Ala	Ser	Phe	Ile	Ala	Gly	Tyr	Gln	Ile	Phe
	2840					2845					2850			
Gln	Ile	Thr	Leu	Thr	Arg	Ser	Tyr	Asn	Val	Thr	Asn	Leu	Thr	Asp
	2855					2860					2865			
Asp	Leu	Lys	Ala	Leu	Tyr	Lys	Val	Ala	Gly	Ala	Asp	Gly	Lys	Gly
	2870					2875					2880			
Ile	Thr	Phe	Ile	Phe	Thr	Asp	Ser	Glu	Ile	Lys	Asp	Glu	Ala	Phe
	2885					2890					2895			
Leu	Glu	Tyr	Leu	Asn	Asn	Leu	Leu	Ser	Ser	Gly	Glu	Ile	Ser	Asn
	2900					2905					2910			
Leu	Phe	Ala	Arg	Asp	Glu	Met	Asp	Glu	Ile	Thr	Gln	Gly	Leu	Ile
	2915					2920					2925			
Ser	Val	Met	Lys	Arg	Glu	Leu	Pro	Arg	His	Pro	Pro	Thr	Phe	Asp
	2930					2935					2940			
Asn	Leu	Tyr	Glu	Tyr	Phe	Ile	Ser	Arg	Ser	Arg	Lys	Asn	Leu	His
	2945					2950					2955			
Val	Val	Leu	Cys	Phe	Ser	Pro	Val	Gly	Glu	Lys	Phe	Arg	Ala	Arg
	2960					2965					2970			

Protein Complexes associated with APP-processing

Ser	Leu	Lys	Phe	Pro	Gly	Leu	Ile	Ser	Gly	Cys	Thr	Met	Asp	Trp
	2975					2980					2985			
Phe	Ser	Arg	Trp	Pro	Arg	Glu	Ala	Leu	Ile	Ala	Val	Ala	Ser	Tyr
	2990					2995					3000			
Phe	Leu	Ser	Asp	Tyr	Asn	Ile	Val	Cys	Ser	Ser	Glu	Ile	Lys	Arg
	3005					3010					3015			
Gln	Val	Val	Glu	Thr	Met	Gly	Leu	Phe	His	Asp	Met	Val	Ser	Glu
	3020					3025					3030			
Ser	Cys	Glu	Ser	Tyr	Phe	Gln	Arg	Tyr	Arg	Arg	Arg	Ala	His	Val
	3035					3040					3045			
Thr	Pro	Lys	Ser	Tyr	Leu	Ser	Phe	Ile	Asn	Gly	Tyr	Lys	Asn	Ile
	3050					3055					3060			
Tyr	Ala	Glu	Lys	Val	Lys	Phe	Ile	Asn	Glu	Gln	Ala	Glu	Arg	Met
	3065					3070					3075			
Asn	Ile	Gly	Leu	Asp	Lys	Leu	Met	Glu	Ala	Ser	Glu	Ser	Val	Ala
	3080					3085					3090			
Lys	Leu	Ser	Gln	Asp	Leu	Ala	Val	Lys	Glu	Lys	Glu	Leu	Ala	Val
	3095					3100					3105			
Ala	Ser	Ile	Lys	Ala	Asp	Glu	Val	Leu	Ala	Glu	Val	Thr	Val	Ser
	3110					3115					3120			
Ala	Gln	Ala	Ser	Ala	Lys	Ile	Lys	Asn	Glu	Val	Gln	Glu	Val	Lys
	3125					3130					3135			
Asp	Lys	Ala	Gln	Lys	Ile	Val	Asp	Glu	Ile	Asp	Ser	Glu	Lys	Val
	3140					3145					3150			
Lys	Ala	Glu	Ser	Lys	Leu	Glu	Ala	Ala	Lys	Pro	Ala	Leu	Glu	Glu
	3155					3160					3165			
Ala	Glu	Ala	Ala	Leu	Asn	Thr	Ile	Lys	Pro	Asn	Asp	Ile	Ala	Thr
	3170					3175					3180			
Val	Arg	Lys	Leu	Ala	Lys	Pro	Pro	His	Leu	Ile	Met	Arg	Ile	Met
	3185					3190					3195			
Asp	Cys	Val	Leu	Leu	Leu	Phe	Gln	Lys	Lys	Ile	Asp	Pro	Val	Thr
	3200					3205					3210			
Met	Asp	Pro	Glu	Lys	Ser	Cys	Cys	Lys	Pro	Ser	Trp	Gly	Glu	Ser
	3215					3220					3225			

Protein Complexes associated with APP-processing

Leu Lys Leu Met Ser Ala Thr Gly Phe Leu Trp Ser Leu Gln Gln
 3230 3235 3240

Phe Pro Lys Asp Thr Ile Asn Glu Glu Thr Val Glu Leu Leu Gln
 3245 3250 3255

Pro Tyr Phe Asn Met Asp Asp Tyr Thr Phe Glu Ser Ala Lys Lys
 3260 3265 3270

Val Cys Gly Asn Val Ala Gly Leu Leu Ser Trp Thr Leu Ala Met
 3275 3280 3285

Ala Ile Phe Tyr Gly Ile Asn Arg Glu Val Leu Pro Leu Lys Ala
 3290 3295 3300

Asn Leu Ala Lys Gln Glu Gly Arg Leu Ala Val Ala Asn Ala Glu
 3305 3310 3315

Leu Gly Lys Ala Gln Ala Leu Leu Asp Glu Lys Gln Ala Glu Leu
 3320 3325 3330

Asp Lys Val Gln Ala Lys Phe Asp Ala Ala Met Asn Glu Lys Met
 3335 3340 3345

Asp Leu Leu Asn Asp Ala Asp Thr Cys Arg Lys Lys Met Gln Ala
 3350 3355 3360

Ala Ser Thr Leu Ile Asp Gly Leu Ser Gly Glu Lys Ile Arg Trp
 3365 3370 3375

Thr Gln Gln Ser Lys Glu Phe Lys Ala Gln Ile Asn Arg Leu Val
 3380 3385 3390

Gly Asp Ile Leu Leu Cys Thr Gly Phe Leu Ser Tyr Leu Gly Pro
 3395 3400 3405

Phe Asn Gln Ile Phe Arg Asn Tyr Leu Leu Lys Asp Gln Trp Glu
 3410 3415 3420

Met Glu Leu Arg Ala Arg Lys Ile Pro Phe Thr Glu Asn Leu Asn
 3425 3430 3435

Leu Ile Ser Met Leu Val Asp Pro Pro Thr Ile Gly Glu Trp Gly
 3440 3445 3450

Leu Gln Gly Leu Pro Gly Asp Asp Leu Ser Ile Gln Asn Gly Ile
 3455 3460 3465

Ile Val Thr Lys Ala Thr Arg Tyr Pro Leu Leu Ile Asp Pro Gln
 3470 3475 3480

Protein Complexes associated with APP-processing

Thr	Gln	Gly	Lys	Thr	Trp	Ile	Lys	Ser	Lys	Glu	Lys	Glu	Asn	Asp
	3485					3490					3495			
Leu	Gln	Val	Thr	Ser	Leu	Asn	His	Lys	Tyr	Phe	Arg	Thr	His	Leu
	3500					3505					3510			
Glu	Asp	Ser	Leu	Ser	Leu	Gly	Arg	Pro	Leu	Leu	Ile	Glu	Asp	Ile
	3515					3520					3525			
His	Glu	Glu	Leu	Asp	Pro	Ala	Leu	Asp	Asn	Val	Leu	Glu	Lys	Asn
	3530					3535					3540			
Phe	Ile	Lys	Ser	Gly	Thr	Thr	Phe	Lys	Val	Lys	Val	Gly	Asp	Lys
	3545					3550					3555			
Glu	Cys	Asp	Ile	Met	Asp	Thr	Phe	Lys	Leu	Tyr	Ile	Thr	Thr	Lys
	3560					3565					3570			
Leu	Pro	Asn	Pro	Ala	Phe	Thr	Pro	Glu	Ile	Asn	Ala	Lys	Thr	Ser
	3575					3580					3585			
Val	Ile	Asp	Phe	Thr	Val	Thr	Met	Lys	Gly	Leu	Glu	Asn	Gln	Leu
	3590					3595					3600			
Leu	Arg	Arg	Val	Ile	Leu	Thr	Glu	Lys	Gln	Glu	Leu	Glu	Ala	Glu
	3605					3610					3615			
Arg	Val	Lys	Leu	Leu	Glu	Asp	Val	Thr	Phe	Asn	Lys	Arg	Lys	Met
	3620					3625					3630			
Lys	Glu	Leu	Glu	Asp	Asn	Leu	Leu	Tyr	Lys	Leu	Ser	Ala	Thr	Lys
	3635					3640					3645			
Gly	Ser	Leu	Val	Asp	Asp	Glu	Ser	Leu	Ile	Gly	Val	Leu	Arg	Thr
	3650					3655					3660			
Thr	Lys	Gln	Thr	Ala	Ala	Glu	Val	Ser	Glu	Lys	Leu	His	Val	Ala
	3665					3670					3675			
Ala	Glu	Thr	Glu	Ile	Lys	Ile	Asn	Ala	Ala	Gln	Glu	Glu	Phe	Arg
	3680					3685					3690			
Pro	Ala	Ala	Thr	Arg	Gly	Ser	Ile	Leu	Tyr	Phe	Leu	Ile	Thr	Glu
	3695					3700					3705			
Met	Ser	Met	Val	Asn	Ile	Met	Tyr	Gln	Thr	Ser	Leu	Ala	Gln	Phe
	3710					3715					3720			
Leu	Lys	Leu	Phe	Asp	Gln	Ser	Met	Ala	Arg	Ser	Glu	Lys	Ser	Pro
	3725					3730					3735			

Protein Complexes associated with APP-processing

Leu Pro Gln Lys Arg Ile Thr Asn Ile Ile Glu Tyr Leu Thr Tyr
 3740 3745 3750

Glu Val Phe Thr Tyr Ser Val Arg Gly Leu Tyr Glu Asn His Lys
 3755 3760 3765

Phe Leu Phe Val Leu Leu Met Thr Leu Lys Ile Asp Leu Gln Arg
 3770 3775 3780

Gly Thr Val Lys His Arg Glu Phe Gln Ala Leu Ile Lys Gly Gly
 3785 3790 3795

Ala Ala Leu Asp Leu Lys Ala Cys Pro Pro Lys Pro Tyr Arg Trp
 3800 3805 3810

Ile Leu Asp Met Thr Trp Leu Asn Leu Val Glu Leu Ser Lys Leu
 3815 3820 3825

Pro Gln Phe Ala Glu Ile Met Asn Gln Ile Ser Arg Asn Glu Lys
 3830 3835 3840

Gly Trp Lys Ser Trp Phe Asp Lys Asp Ala Pro Glu Glu Glu Ile
 3845 3850 3855

Ile Pro Asp Gly Tyr Asn Asp Ser Leu Asp Thr Cys His Lys Leu
 3860 3865 3870

Leu Leu Ile Arg Ser Trp Cys Pro Asp Arg Thr Val Phe Gln Ala
 3875 3880 3885

Arg Lys Tyr Ile Ala Asp Ser Leu Glu Glu Lys Tyr Thr Glu Pro
 3890 3895 3900

Val Ile Leu Asn Leu Glu Lys Thr Trp Glu Glu Ser Asp Thr Arg
 3905 3910 3915

Thr Pro Leu Ile Cys Phe Leu Ser Met Gly Ser Asp Pro Thr Asn
 3920 3925 3930

Gln Ile Asp Ala Leu Ala Lys Lys Leu Lys Leu Glu Cys Arg Thr
 3935 3940 3945

Ile Ser Met Gly Gln Gly Gln Glu Val His Ala Arg Lys Leu Ile
 3950 3955 3960

Gln Met Ser Met Gln Gln Gly Gly Trp Val Leu Leu Gln Asn Cys
 3965 3970 3975

His Leu Gly Leu Glu Phe Met Glu Glu Leu Leu Glu Thr Leu Ile
 3980 3985 3990

Protein Complexes associated with APP-processing

Thr	Thr	Glu	Ala	Ser	Asp	Asp	Ser	Phe	Arg	Val	Trp	Ile	Thr	Thr
	3995					4000					4005			
Glu	Pro	His	Asp	Arg	Phe	Pro	Ile	Thr	Leu	Leu	Gln	Thr	Ser	Leu
	4010					4015					4020			
Lys	Phe	Thr	Asn	Glu	Pro	Pro	Gln	Gly	Val	Arg	Ala	Gly	Leu	Lys
	4025					4030					4035			
Arg	Thr	Phe	Ala	Gly	Ile	Asn	Gln	Asp	Leu	Leu	Asp	Ile	Ser	Asn
	4040					4045					4050			
Leu	Pro	Met	Trp	Lys	Pro	Met	Leu	Tyr	Thr	Val	Ala	Phe	Leu	His
	4055					4060					4065			
Ser	Thr	Val	Gln	Glu	Arg	Arg	Lys	Phe	Gly	Pro	Leu	Gly	Trp	Asn
	4070					4075					4080			
Ile	Pro	Tyr	Glu	Phe	Asn	Ser	Ala	Asp	Phe	Ser	Ala	Ser	Val	Gln
	4085					4090					4095			
Phe	Ile	Gln	Asn	His	Leu	Asp	Glu	Cys	Asp	Ile	Lys	Lys	Gly	Val
	4100					4105					4110			
Ser	Trp	Asn	Thr	Val	Arg	Tyr	Met	Ile	Gly	Glu	Val	Gln	Tyr	Gly
	4115					4120					4125			
Gly	Arg	Val	Thr	Asp	Asp	Phe	Asp	Lys	Arg	Leu	Leu	Asn	Cys	Phe
	4130					4135					4140			
Ala	Arg	Val	Trp	Phe	Ser	Glu	Lys	Met	Phe	Glu	Pro	Ser	Phe	Cys
	4145					4150					4155			
Phe	Tyr	Thr	Gly	Tyr	Lys	Ile	Pro	Leu	Cys	Lys	Thr	Leu	Asp	Gln
	4160					4165					4170			
Tyr	Phe	Glu	Tyr	Ile	Gln	Ser	Leu	Pro	Ser	Leu	Asp	Asn	Pro	Glu
	4175					4180					4185			
Val	Phe	Gly	Leu	His	Pro	Asn	Ala	Asp	Ile	Thr	Tyr	Gln	Ser	Asn
	4190					4195					4200			
Thr	Ala	Ser	Ala	Val	Leu	Glu	Thr	Ile	Thr	Asn	Ile	Gln	Pro	Lys
	4205					4210					4215			
Glu	Ser	Gly	Gly	Gly	Val	Gly	Glu	Thr	Arg	Glu	Ala	Ile	Val	Tyr
	4220					4225					4230			
Arg	Leu	Ser	Glu	Asp	Met	Leu	Ser	Lys	Leu	Pro	Pro	Asp	Tyr	Ile
	4235					4240					4245			

Protein Complexes associated with APP-processing

Pro His Glu Val Lys Ser Arg Leu Ile Lys Met Gly His Leu Asn
4250 4255 4260

Ser Met Asn Ile Phe Leu Arg Gln Glu Ile Asp Arg Met Gln Arg
4265 4270 4275

Val Ile Ser Ile Leu Arg Ser Ser Leu Ser Asp Leu Lys Leu Ala
4280 4285 4290

Ile Glu Gly Thr Ile Ile Met Ser Glu Asn Leu Arg Asp Ala Leu
4295 4300 4305

Asp Asn Met Tyr Asp Ala Arg Ile Pro Gln Leu Trp Lys Arg Val
4310 4315 4320

Ser Trp Asp Ser Ser Thr Leu Gly Phe Trp Phe Thr Glu Leu Leu
4325 4330 4335

Glu Arg Asn Ala Gln Phe Ser Thr Trp Ile Phe Glu Gly Arg Pro
4340 4345 4350

Asn Val Phe Trp Met Thr Gly Phe Phe Asn Pro Gln Gly Phe Leu
4355 4360 4365

Thr Ala Met Arg Gln Glu Val Thr Arg Ala His Lys Gly Trp Ala
4370 4375 4380

Leu Asp Thr Val Thr Ile His Asn Glu Val Leu Arg Gln Thr Lys
4385 4390 4395

Glu Glu Ile Thr Ser Pro Pro Gly Glu Gly Val Tyr Ile Tyr Gly
4400 4405 4410

Leu Tyr Met Asp Gly Ala Ala Trp Asp Arg Arg Asn Gly Lys Leu
4415 4420 4425

Met Glu Ser Thr Pro Lys Val Leu Phe Thr Gln Leu Pro Val Leu
4430 4435 4440

His Ile Phe Ala Ile Asn Ser Thr Ala Pro Lys Asp Pro Lys Leu
4445 4450 4455

Tyr Val Cys Pro Ile Tyr Lys Lys Pro Arg Arg Thr Asp Leu Thr
4460 4465 4470

Phe Ile Thr Val Val Tyr Leu Arg Thr Val Leu Ser Pro Asp His
4475 4480 4485

Trp Ile Leu Arg Gly Val Ala Leu Leu Cys Asp Ile Lys
4490 4495 4500

Protein Complexes associated with APP-processing

<210> 46

<211> 2923

<212> PRT

<213> Homo sapiens

<400> 46

Met Arg Ser Pro Ala Thr Gly Val Pro Leu Pro Thr Pro Pro Pro Pro
 1 5 10 15

Leu Leu Leu Leu Leu Leu Leu Leu Leu Pro Pro Pro Leu Leu Gly Asp
 20 25 30

Gln Val Gly Pro Cys Arg Ser Leu Gly Ser Arg Gly Arg Gly Ser Ser
 35 40 45

Gly Ala Cys Ala Pro Met Gly Trp Leu Cys Pro Ser Ser Ala Ser Asn
 50 55 60

Leu Trp Leu Tyr Thr Ser Arg Cys Arg Asp Ala Gly Thr Glu Leu Thr
 65 70 75 80

Gly His Leu Val Pro His His Asp Gly Leu Arg Val Trp Cys Pro Glu
 85 90 95

Ser Glu Ala His Ile Pro Leu Pro Pro Ala Pro Glu Gly Cys Pro Trp
 100 105 110

Ser Cys Arg Leu Leu Gly Ile Gly Gly His Leu Ser Pro Gln Gly Lys
 115 120 125

Leu Thr Leu Pro Glu Glu His Pro Cys Leu Lys Ala Pro Arg Leu Arg
 130 135 140

Cys Gln Ser Cys Lys Leu Ala Gln Ala Pro Gly Leu Arg Ala Gly Glu
 145 150 155 160

Arg Ser Pro Glu Glu Ser Leu Gly Gly Arg Arg Lys Arg Asn Val Asn
 165 170 175

Thr Ala Pro Gln Phe Gln Pro Pro Ser Tyr Gln Ala Thr Val Pro Glu
 180 185 190

Asn Gln Pro Ala Gly Thr Pro Val Ala Ser Leu Arg Ala Ile Asp Pro
 195 200 205

Asp Glu Gly Glu Ala Gly Arg Leu Glu Tyr Thr Met Asp Ala Leu Phe
 210 215 220

Protein Complexes associated with APP-processing

Asp Ser Arg Ser Asn Gln Phe Phe Ser Leu Asp Pro Val Thr Gly Ala
 225 230 235 240

Val Thr Thr Ala Glu Glu Leu Asp Arg Glu Thr Lys Ser Thr His Val
 245 250 255

Phe Arg Val Thr Ala Gln Asp His Gly Met Pro Arg Arg Ser Ala Leu
 260 265 270

Ala Thr Leu Thr Ile Leu Val Thr Asp Thr Asn Asp His Asp Pro Val
 275 280 285

Phe Glu Gln Gln Glu Tyr Lys Glu Ser Leu Arg Glu Asn Leu Glu Val
 290 295 300

Gly Tyr Glu Val Leu Thr Val Arg Ala Thr Asp Gly Asp Ala Pro Pro
 305 310 315 320

Asn Ala Asn Ile Leu Tyr Arg Leu Leu Glu Gly Ser Gly Gly Ser Pro
 325 330 335

Ser Glu Val Phe Glu Ile Asp Pro Arg Ser Gly Val Ile Arg Thr Arg
 340 345 350

Gly Pro Val Asp Arg Glu Glu Val Glu Ser Tyr Gln Leu Thr Val Glu
 355 360 365

Ala Ser Asp Gln Gly Arg Asp Pro Gly Pro Arg Ser Thr Thr Ala Ala
 370 375 380

Val Phe Leu Ser Val Glu Asp Asp Asn Asp Asn Ala Pro Gln Phe Ser
 385 390 395 400

Glu Lys Arg Tyr Val Val Gln Val Arg Glu Asp Val Thr Pro Gly Ala
 405 410 415

Pro Val Leu Arg Val Thr Ala Ser Asp Arg Asp Lys Gly Ser Asn Ala
 420 425 430

Val Val His Tyr Ser Ile Met Ser Gly Asn Ala Arg Gly Gln Phe Tyr
 435 440 445

Leu Asp Ala Gln Thr Gly Ala Leu Asp Val Val Ser Pro Leu Asp Tyr
 450 455 460

Glu Thr Thr Lys Glu Tyr Thr Leu Arg Val Arg Ala Gln Asp Gly Gly
 465 470 475 480

Arg Pro Pro Leu Ser Asn Val Ser Gly Leu Val Thr Val Gln Val Leu
 485 490 495

Protein Complexes associated with APP-processing
 Thr Gln Ala Glu Leu Asp Tyr Glu Asp Gln Val Ser Tyr Thr Leu Ala
 770 775 780

Ile Thr Ala Arg Asp Asn Gly Ile Pro Gln Lys Ser Asp Thr Thr Tyr
 785 790 795 800

Leu Glu Ile Leu Val Asn Asp Val Asn Asp Asn Ala Pro Gln Phe Leu
 805 810 815

Arg Asp Ser Tyr Gln Gly Ser Val Tyr Glu Asp Val Pro Pro Phe Thr
 820 825 830

Ser Val Leu Gln Ile Ser Ala Thr Asp Arg Asp Ser Gly Leu Asn Gly
 835 840 845

Arg Val Phe Tyr Thr Phe Gln Gly Gly Asp Asp Gly Asp Gly Asp Phe
 850 855 860

Ile Val Glu Ser Thr Ser Gly Ile Val Arg Thr Leu Arg Arg Leu Asp
 865 870 875 880

Arg Glu Asn Val Ala Gln Tyr Val Leu Arg Ala Tyr Ala Val Asp Lys
 885 890 895

Gly Met Pro Pro Ala Arg Thr Pro Met Glu Val Thr Val Thr Val Leu
 900 905 910

Asp Val Asn Asp Asn Pro Pro Val Phe Glu Gln Asp Glu Phe Asp Val
 915 920 925

Phe Val Glu Glu Asn Ser Pro Ile Gly Leu Ala Val Ala Arg Val Thr
 930 935 940

Ala Thr Asp Pro Asp Glu Gly Thr Asn Ala Gln Ile Met Tyr Gln Ile
 945 950 955 960

Val Glu Gly Asn Ile Pro Glu Val Phe Gln Leu Asp Ile Phe Ser Gly
 965 970 975

Glu Leu Thr Ala Leu Val Asp Leu Asp Tyr Glu Asp Arg Pro Glu Tyr
 980 985 990

Val Leu Val Ile Gln Ala Thr Ser Ala Pro Leu Val Ser Arg Ala Thr
 995 1000 1005

Val His Val Arg Leu Leu Asp Arg Asn Asp Asn Pro Pro Val Leu
 1010 1015 1020

Gly Asn Phe Glu Ile Leu Phe Asn Asn Tyr Val Thr Asn Arg Ser
 1025 1030 1035

Protein Complexes associated with APP-processing

Ser Ser Phe Pro Gly Gly Ala Ile Gly Arg Val Pro Ala His Asp
 1040 1045 1050

Pro Asp Ile Ser Asp Ser Leu Thr Tyr Ser Phe Glu Arg Gly Asn
 1055 1060 1065

Glu Leu Ser Leu Val Leu Leu Asn Ala Ser Thr Gly Glu Leu Lys
 1070 1075 1080

Leu Ser Arg Ala Leu Asp Asn Asn Arg Pro Leu Glu Ala Ile Met
 1085 1090 1095

Ser Val Leu Val Ser Asp Gly Val His Ser Val Thr Ala Gln Cys
 1100 1105 1110

Ala Leu Arg Val Thr Ile Ile Thr Asp Glu Met Leu Thr His Ser
 1115 1120 1125

Ile Thr Leu Arg Leu Glu Asp Met Ser Pro Glu Arg Phe Leu Ser
 1130 1135 1140

Pro Leu Leu Gly Leu Phe Ile Gln Ala Val Ala Ala Thr Leu Ala
 1145 1150 1155

Thr Pro Pro Asp His Val Val Val Phe Asn Val Gln Arg Asp Thr
 1160 1165 1170

Asp Ala Pro Gly Gly His Ile Leu Asn Val Ser Leu Ser Val Gly
 1175 1180 1185

Gln Pro Pro Gly Pro Gly Gly Gly Pro Pro Phe Leu Pro Ser Glu
 1190 1195 1200

Asp Leu Gln Glu Arg Leu Tyr Leu Asn Arg Ser Leu Leu Thr Ala
 1205 1210 1215

Ile Ser Ala Gln Arg Val Leu Pro Phe Asp Asp Asn Ile Cys Leu
 1220 1225 1230

Arg Glu Pro Cys Glu Asn Tyr Met Arg Cys Val Ser Val Leu Arg
 1235 1240 1245

Phe Asp Ser Ser Ala Pro Phe Ile Ala Ser Ser Ser Val Leu Phe
 1250 1255 1260

Arg Pro Ile His Pro Val Gly Gly Leu Arg Cys Arg Cys Pro Pro
 1265 1270 1275

Gly Phe Thr Gly Asp Tyr Cys Glu Thr Glu Val Asp Leu Cys Tyr
 1280 1285 1290

Protein Complexes associated with APP-processing

Ser	Arg	Pro	Cys	Gly	Pro	His	Gly	Arg	Cys	Arg	Ser	Arg	Glu	Gly
1295						1300					1305			
Gly	Tyr	Thr	Cys	Leu	Cys	Arg	Asp	Gly	Tyr	Thr	Gly	Glu	His	Cys
1310						1315					1320			
Glu	Val	Ser	Ala	Arg	Ser	Gly	Arg	Cys	Thr	Pro	Gly	Val	Cys	Lys
1325						1330					1335			
Asn	Gly	Gly	Thr	Cys	Val	Asn	Leu	Leu	Val	Gly	Gly	Phe	Lys	Cys
1340						1345					1350			
Asp	Cys	Pro	Ser	Gly	Asp	Phe	Glu	Lys	Pro	Tyr	Cys	Gln	Val	Thr
1355						1360					1365			
Thr	Arg	Ser	Phe	Pro	Ala	His	Ser	Phe	Ile	Thr	Phe	Arg	Gly	Leu
1370						1375					1380			
Arg	Gln	Arg	Phe	His	Phe	Thr	Leu	Ala	Leu	Ser	Phe	Ala	Thr	Lys
1385						1390					1395			
Glu	Arg	Asp	Gly	Leu	Leu	Leu	Tyr	Asn	Gly	Arg	Phe	Asn	Glu	Lys
1400						1405					1410			
His	Asp	Phe	Val	Ala	Leu	Glu	Val	Ile	Gln	Glu	Gln	Val	Gln	Leu
1415						1420					1425			
Thr	Phe	Ser	Ala	Gly	Glu	Ser	Thr	Thr	Thr	Val	Ser	Pro	Phe	Val
1430						1435					1440			
Pro	Gly	Gly	Val	Ser	Asp	Gly	Gln	Trp	His	Thr	Val	Gln	Leu	Lys
1445						1450					1455			
Tyr	Tyr	Asn	Lys	Pro	Leu	Leu	Gly	Gln	Thr	Gly	Leu	Pro	Gln	Gly
1460						1465					1470			
Pro	Ser	Glu	Gln	Lys	Val	Ala	Val	Val	Thr	Val	Asp	Gly	Cys	Asp
1475						1480					1485			
Thr	Gly	Val	Ala	Leu	Arg	Phe	Gly	Ser	Val	Leu	Gly	Asn	Tyr	Ser
1490						1495					1500			
Cys	Ala	Ala	Gln	Gly	Thr	Gln	Gly	Gly	Ser	Lys	Lys	Ser	Leu	Asp
1505						1510					1515			
Leu	Thr	Gly	Pro	Leu	Leu	Leu	Gly	Gly	Val	Pro	Asp	Leu	Pro	Glu
1520						1525					1530			
Ser	Phe	Pro	Val	Arg	Met	Arg	Gln	Phe	Val	Gly	Cys	Met	Arg	Asn
1535						1540					1545			

Protein Complexes associated with APP-processing

Leu	Gln	Val	Asp	Ser	Arg	His	Ile	Asp	Met	Ala	Asp	Phe	Ile	Ala
	1550					1555					1560			
Asn	Asn	Gly	Thr	Val	Pro	Gly	Cys	Pro	Ala	Lys	Lys	Asn	Val	Cys
	1565					1570					1575			
Asp	Ser	Asn	Thr	Cys	His	Asn	Gly	Gly	Thr	Cys	Val	Asn	Gln	Trp
	1580					1585					1590			
Asp	Ala	Phe	Ser	Cys	Glu	Cys	Pro	Leu	Gly	Phe	Gly	Gly	Lys	Ser
	1595					1600					1605			
Cys	Ala	Gln	Glu	Met	Ala	Asn	Pro	Gln	His	Phe	Leu	Gly	Ser	Ser
	1610					1615					1620			
Leu	Val	Ala	Trp	His	Gly	Leu	Ser	Leu	Pro	Ile	Ser	Gln	Pro	Trp
	1625					1630					1635			
Tyr	Leu	Ser	Leu	Met	Phe	Arg	Thr	Arg	Gln	Ala	Asp	Gly	Val	Leu
	1640					1645					1650			
Leu	Gln	Ala	Ile	Thr	Arg	Gly	Arg	Ser	Thr	Ile	Thr	Leu	Gln	Leu
	1655					1660					1665			
Arg	Glu	Gly	His	Val	Met	Leu	Ser	Val	Glu	Gly	Thr	Gly	Leu	Gln
	1670					1675					1680			
Ala	Ser	Ser	Leu	Arg	Leu	Glu	Pro	Gly	Arg	Ala	Asn	Asp	Gly	Asp
	1685					1690					1695			
Trp	His	His	Ala	Gln	Leu	Ala	Leu	Gly	Ala	Ser	Gly	Gly	Pro	Gly
	1700					1705					1710			
His	Ala	Ile	Leu	Ser	Phe	Asp	Tyr	Gly	Gln	Gln	Arg	Ala	Glu	Gly
	1715					1720					1725			
Asn	Leu	Gly	Pro	Arg	Leu	His	Gly	Leu	His	Leu	Ser	Asn	Ile	Thr
	1730					1735					1740			
Val	Gly	Gly	Ile	Pro	Gly	Pro	Ala	Gly	Gly	Val	Ala	Arg	Gly	Phe
	1745					1750					1755			
Arg	Gly	Cys	Leu	Gln	Gly	Val	Arg	Val	Ser	Asp	Thr	Pro	Glu	Gly
	1760					1765					1770			
Val	Asn	Ser	Leu	Asp	Pro	Ser	His	Gly	Glu	Ser	Ile	Asn	Val	Glu
	1775					1780					1785			
Gln	Gly	Cys	Ser	Leu	Pro	Asp	Pro	Cys	Asp	Ser	Asn	Pro	Cys	Pro
	1790					1795					1800			

Protein Complexes associated with APP-processing

Ala	Asn	Ser	Tyr	Cys	Ser	Asn	Asp	Trp	Asp	Ser	Tyr	Ser	Cys	Ser
	1805					1810					1815			
Cys	Asp	Pro	Gly	Tyr	Tyr	Gly	Asp	Asn	Cys	Thr	Asn	Val	Cys	Asp
	1820					1825					1830			
Leu	Asn	Pro	Cys	Glu	His	Gln	Ser	Val	Cys	Thr	Arg	Lys	Pro	Ser
	1835					1840					1845			
Ala	Pro	His	Gly	Tyr	Thr	Cys	Glu	Cys	Pro	Pro	Asn	Tyr	Leu	Gly
	1850					1855					1860			
Pro	Tyr	Cys	Glu	Thr	Arg	Ile	Asp	Gln	Pro	Cys	Pro	Arg	Gly	Trp
	1865					1870					1875			
Trp	Gly	His	Pro	Thr	Cys	Gly	Pro	Cys	Asn	Cys	Asp	Val	Ser	Lys
	1880					1885					1890			
Gly	Phe	Asp	Pro	Asp	Cys	Asn	Lys	Thr	Ser	Gly	Glu	Cys	His	Cys
	1895					1900					1905			
Lys	Glu	Asn	His	Tyr	Arg	Pro	Pro	Gly	Ser	Pro	Thr	Cys	Leu	Leu
	1910					1915					1920			
Cys	Asp	Cys	Tyr	Pro	Thr	Gly	Ser	Leu	Ser	Arg	Val	Cys	Asp	Pro
	1925					1930					1935			
Glu	Asp	Gly	Gln	Cys	Pro	Cys	Lys	Pro	Gly	Val	Ile	Gly	Arg	Gln
	1940					1945					1950			
Cys	Asp	Arg	Cys	Asp	Asn	Pro	Phe	Ala	Glu	Val	Thr	Thr	Asn	Gly
	1955					1960					1965			
Cys	Glu	Val	Asn	Tyr	Asp	Ser	Cys	Pro	Arg	Ala	Ile	Glu	Ala	Gly
	1970					1975					1980			
Ile	Trp	Trp	Pro	Arg	Thr	Arg	Phe	Gly	Leu	Pro	Ala	Ala	Ala	Pro
	1985					1990					1995			
Cys	Pro	Lys	Gly	Ser	Phe	Gly	Thr	Ala	Val	Arg	His	Cys	Asp	Glu
	2000					2005					2010			
His	Arg	Gly	Trp	Leu	Pro	Pro	Asn	Leu	Phe	Asn	Cys	Thr	Ser	Ile
	2015					2020					2025			
Thr	Phe	Ser	Glu	Leu	Lys	Gly	Phe	Ala	Glu	Arg	Leu	Gln	Arg	Asn
	2030					2035					2040			
Glu	Ser	Gly	Leu	Asp	Ser	Gly	Arg	Ser	Gln	Gln	Leu	Ala	Leu	Leu
	2045					2050					2055			

Protein Complexes associated with APP-processing

Leu	Arg	Asn	Ala	Thr	Gln	His	Thr	Ala	Gly	Tyr	Phe	Gly	Ser	Asp
	2060					2065					2070			
Val	Lys	Val	Ala	Tyr	Gln	Leu	Ala	Thr	Arg	Leu	Leu	Ala	His	Glu
	2075					2080					2085			
Ser	Thr	Gln	Arg	Gly	Phe	Gly	Leu	Ser	Ala	Thr	Gln	Asp	Val	His
	2090					2095					2100			
Phe	Thr	Glu	Asn	Leu	Leu	Arg	Val	Gly	Ser	Ala	Leu	Leu	Asp	Thr
	2105					2110					2115			
Ala	Asn	Lys	Arg	His	Trp	Glu	Leu	Ile	Gln	Gln	Thr	Glu	Gly	Gly
	2120					2125					2130			
Thr	Ala	Trp	Leu	Leu	Gln	His	Tyr	Glu	Ala	Tyr	Ala	Ser	Ala	Leu
	2135					2140					2145			
Ala	Gln	Asn	Met	Arg	His	Thr	Tyr	Leu	Ser	Pro	Phe	Thr	Ile	Val
	2150					2155					2160			
Thr	Pro	Asn	Ile	Val	Ile	Ser	Val	Val	Arg	Leu	Asp	Lys	Gly	Asn
	2165					2170					2175			
Phe	Ala	Gly	Ala	Lys	Leu	Pro	Arg	Tyr	Glu	Ala	Leu	Arg	Gly	Glu
	2180					2185					2190			
Gln	Pro	Pro	Asp	Leu	Glu	Thr	Thr	Val	Ile	Leu	Pro	Glu	Ser	Val
	2195					2200					2205			
Phe	Arg	Glu	Thr	Pro	Pro	Val	Val	Arg	Pro	Ala	Gly	Pro	Gly	Glu
	2210					2215					2220			
Ala	Gln	Glu	Pro	Glu	Glu	Leu	Ala	Arg	Arg	Gln	Arg	Arg	His	Pro
	2225					2230					2235			
Glu	Leu	Ser	Gln	Gly	Glu	Ala	Val	Ala	Ser	Val	Ile	Ile	Tyr	Arg
	2240					2245					2250			
Thr	Leu	Ala	Gly	Leu	Leu	Pro	His	Asn	Tyr	Asp	Pro	Asp	Lys	Arg
	2255					2260					2265			
Ser	Leu	Arg	Val	Pro	Lys	Arg	Pro	Ile	Ile	Asn	Thr	Pro	Val	Val
	2270					2275					2280			
Ser	Ile	Ser	Val	His	Asp	Asp	Glu	Glu	Leu	Leu	Pro	Arg	Ala	Leu
	2285					2290					2295			
Asp	Lys	Pro	Val	Thr	Val	Gln	Phe	Arg	Leu	Leu	Glu	Thr	Glu	Glu
	2300					2305					2310			

Protein Complexes associated with APP-processing

Arg	Thr	Lys	Pro	Ile	Cys	Val	Phe	Trp	Asn	His	Ser	Ile	Leu	Val
2315						2320					2325			
Ser	Gly	Thr	Gly	Gly	Trp	Ser	Ala	Arg	Gly	Cys	Glu	Val	Val	Phe
2330						2335					2340			
Arg	Asn	Glu	Ser	His	Val	Ser	Cys	Gln	Cys	Asn	His	Met	Thr	Ser
2345						2350					2355			
Phe	Ala	Val	Leu	Met	Asp	Val	Ser	Arg	Arg	Glu	Asn	Gly	Glu	Ile
2360						2365					2370			
Leu	Pro	Leu	Lys	Thr	Leu	Thr	Tyr	Val	Ala	Leu	Gly	Val	Thr	Leu
2375						2380					2385			
Ala	Ala	Leu	Leu	Leu	Thr	Phe	Phe	Phe	Leu	Thr	Leu	Leu	Arg	Ile
2390						2395					2400			
Leu	Arg	Ser	Asn	Gln	His	Gly	Ile	Arg	Arg	Asn	Leu	Thr	Ala	Ala
2405						2410					2415			
Leu	Gly	Leu	Ala	Gln	Leu	Val	Phe	Leu	Leu	Gly	Ile	Asn	Gln	Ala
2420						2425					2430			
Asp	Leu	Pro	Phe	Ala	Cys	Thr	Val	Ile	Ala	Ile	Leu	Leu	His	Phe
2435						2440					2445			
Leu	Tyr	Leu	Cys	Thr	Phe	Ser	Trp	Ala	Leu	Leu	Glu	Ala	Leu	His
2450						2455					2460			
Leu	Tyr	Arg	Ala	Leu	Thr	Glu	Val	Arg	Asp	Val	Asn	Thr	Gly	Pro
2465						2470					2475			
Met	Arg	Phe	Tyr	Tyr	Met	Leu	Gly	Trp	Gly	Val	Pro	Ala	Phe	Ile
2480						2485					2490			
Thr	Gly	Leu	Ala	Val	Gly	Leu	Asp	Pro	Glu	Gly	Tyr	Gly	Asn	Pro
2495						2500					2505			
Asp	Phe	Cys	Trp	Leu	Ser	Ile	Tyr	Asp	Thr	Leu	Ile	Trp	Ser	Phe
2510						2515					2520			
Ala	Gly	Pro	Val	Ala	Phe	Ala	Val	Ser	Met	Ser	Val	Phe	Leu	Tyr
2525						2530					2535			
Ile	Leu	Ala	Ala	Arg	Ala	Ser	Cys	Ala	Ala	Gln	Arg	Gln	Gly	Phe
2540						2545					2550			
Glu	Lys	Lys	Gly	Pro	Val	Ser	Gly	Leu	Gln	Pro	Ser	Phe	Ala	Val
2555						2560					2565			

Protein Complexes associated with APP-processing

Leu	Leu	Leu	Leu	Ser	Ala	Thr	Trp	Leu	Leu	Ala	Leu	Leu	Ser	Val
	2570					2575					2580			
Asn	Ser	Asp	Thr	Leu	Leu	Phe	His	Tyr	Leu	Phe	Ala	Thr	Cys	Asn
	2585					2590					2595			
Cys	Ile	Gln	Gly	Pro	Phe	Ile	Phe	Leu	Ser	Tyr	Val	Val	Leu	Ser
	2600					2605					2610			
Lys	Glu	Val	Arg	Lys	Ala	Leu	Lys	Leu	Ala	Cys	Ser	Arg	Lys	Pro
	2615					2620					2625			
Ser	Pro	Asp	Pro	Ala	Leu	Thr	Thr	Lys	Ser	Thr	Leu	Thr	Ser	Ser
	2630					2635					2640			
Tyr	Asn	Cys	Pro	Ser	Pro	Tyr	Ala	Asp	Gly	Arg	Leu	Tyr	Gln	Pro
	2645					2650					2655			
Tyr	Gly	Asp	Ser	Ala	Gly	Ser	Leu	His	Ser	Thr	Ser	Arg	Ser	Gly
	2660					2665					2670			
Lys	Ser	Gln	Pro	Ser	Tyr	Ile	Pro	Phe	Leu	Leu	Arg	Glu	Glu	Ser
	2675					2680					2685			
Ala	Leu	Asn	Pro	Gly	Gln	Gly	Pro	Pro	Gly	Leu	Gly	Asp	Pro	Gly
	2690					2695					2700			
Ser	Leu	Phe	Leu	Glu	Gly	Gln	Asp	Gln	Gln	His	Asp	Pro	Asp	Thr
	2705					2710					2715			
Asp	Ser	Asp	Ser	Asp	Leu	Ser	Leu	Glu	Asp	Asp	Gln	Ser	Gly	Ser
	2720					2725					2730			
Tyr	Ala	Ser	Thr	His	Ser	Ser	Asp	Ser	Glu	Glu	Glu	Glu	Glu	Glu
	2735					2740					2745			
Glu	Glu	Glu	Glu	Ala	Ala	Phe	Pro	Gly	Glu	Gln	Gly	Trp	Asp	Ser
	2750					2755					2760			
Leu	Leu	Gly	Pro	Gly	Ala	Glu	Arg	Leu	Pro	Leu	His	Ser	Thr	Pro
	2765					2770					2775			
Lys	Asp	Gly	Gly	Pro	Gly	Pro	Gly	Lys	Ala	Pro	Trp	Pro	Gly	Asp
	2780					2785					2790			
Phe	Gly	Thr	Thr	Ala	Lys	Glu	Ser	Ser	Gly	Asn	Gly	Ala	Pro	Glu
	2795					2800					2805			
Glu	Arg	Leu	Arg	Glu	Asn	Gly	Asp	Ala	Leu	Ser	Arg	Glu	Gly	Ser
	2810					2815					2820			

Protein Complexes associated with APP-processing
 Leu Gly Pro Leu Pro Gly Ser Ser Ala Gln Pro His Lys Gly Ile
 2825 2830 2835

Leu Lys Lys Lys Cys Leu Pro Thr Ile Ser Glu Lys Ser Ser Leu
 2840 2845 2850

Leu Arg Leu Pro Leu Glu Gln Cys Thr Gly Ser Ser Arg Gly Ser
 2855 2860 2865

Ser Ala Ser Glu Gly Ser Arg Gly Gly Pro Pro Pro Arg Pro Pro
 2870 2875 2880

Pro Arg Gln Ser Leu Gln Glu Gln Leu Asn Gly Val Met Pro Ile
 2885 2890 2895

Ala Met Ser Ile Lys Ala Gly Thr Val Asp Glu Asp Ser Ser Gly
 2900 2905 2910

Ser Glu Phe Leu Phe Phe Asn Phe Leu His
 2915 2920

<210> 47

<211> 981

<212> PRT

<213> Homo sapiens

<400> 47

Met Leu Arg Arg Pro Ala Pro Ala Leu Ala Pro Ala Ala Arg Leu Leu
 1 5 10 15

Leu Ala Gly Leu Leu Cys Gly Gly Gly Val Trp Ala Ala Arg Val Asn
 20 25 30

Lys His Lys Pro Trp Leu Glu Pro Thr Tyr His Gly Ile Val Thr Glu
 35 40 45

Asn Asp Asn Thr Val Leu Leu Asp Pro Pro Leu Ile Ala Leu Asp Lys
 50 55 60

Asp Ala Pro Leu Arg Phe Ala Glu Ser Phe Glu Val Thr Val Thr Lys
 65 70 75 80

Glu Gly Glu Ile Cys Gly Phe Lys Ile His Gly Gln Asn Val Pro Phe
 85 90 95

Asp Ala Val Val Val Asp Lys Ser Thr Gly Glu Gly Val Ile Arg Ser
 100 105 110

Protein Complexes associated with APP-processing

Lys Glu Lys Leu Asp Cys Glu Leu Gln Lys Asp Tyr Ser Phe Thr Ile
 115 120 125

Gln Ala Tyr Asp Cys Gly Lys Gly Pro Asp Gly Thr Asn Val Lys Lys
 130 135 140

Ser His Lys Ala Thr Val His Ile Gln Val Asn Asp Val Asn Glu Tyr
 145 150 155 160

Ala Pro Val Phe Lys Glu Lys Ser Tyr Lys Ala Thr Val Ile Glu Gly
 165 170 175

Lys Gln Tyr Asp Ser Ile Leu Arg Val Glu Ala Val Asp Ala Asp Cys
 180 185 190

Ser Pro Gln Phe Ser Gln Ile Cys Ser Tyr Glu Ile Ile Thr Pro Asp
 195 200 205

Val Pro Phe Thr Val Asp Lys Asp Gly Tyr Ile Lys Asn Thr Glu Lys
 210 215 220

Leu Asn Tyr Gly Lys Glu His Gln Tyr Lys Leu Thr Val Thr Ala Tyr
 225 230 235 240

Asp Cys Gly Lys Lys Arg Ala Thr Glu Asp Val Leu Val Lys Ile Ser
 245 250 255

Ile Lys Pro Thr Cys Thr Pro Gly Trp Gln Gly Trp Asn Asn Arg Ile
 260 265 270

Glu Tyr Glu Pro Gly Thr Gly Ala Leu Ala Val Phe Pro Asn Ile His
 275 280 285

Leu Glu Thr Cys Asp Glu Pro Val Ala Ser Val Gln Ala Thr Val Glu
 290 295 300

Leu Glu Thr Ser His Ile Gly Lys Gly Cys Asp Arg Asp Thr Tyr Ser
 305 310 315 320

Glu Lys Ser Leu His Arg Leu Cys Gly Ala Ala Ala Gly Thr Ala Glu
 325 330 335

Leu Leu Pro Ser Pro Ser Gly Ser Leu Asn Trp Thr Met Gly Leu Pro
 340 345 350

Thr Asp Asn Gly His Asp Ser Asp Gln Val Phe Glu Phe Asn Gly Thr
 355 360 365

Gln Ala Val Arg Ile Pro Asp Gly Val Val Ser Val Ser Pro Lys Glu
 370 375 380

Protein Complexes associated with APP-processing

Pro Phe Thr Ile Ser Val Trp Met Arg His Gly Pro Phe Gly Arg Lys
 385 390 395 400

Lys Glu Thr Ile Leu Cys Ser Ser Asp Lys Thr Asp Met Asn Arg His
 405 410 415

His Tyr Ser Leu Tyr Val His Gly Cys Arg Leu Ile Phe Leu Phe Arg
 420 425 430

Gln Asp Pro Ser Glu Glu Lys Lys Tyr Arg Pro Ala Glu Phe His Trp
 435 440 445

Lys Leu Asn Gln Val Cys Asp Glu Glu Trp His His Tyr Val Leu Asn
 450 455 460

Val Glu Phe Pro Ser Val Thr Leu Tyr Val Asp Gly Thr Ser His Glu
 465 470 475 480

Pro Phe Ser Val Thr Glu Asp Tyr Pro Leu His Pro Ser Lys Ile Glu
 485 490 495

Thr Gln Leu Val Val Gly Ala Cys Trp Gln Glu Phe Ser Gly Val Glu
 500 505 510

Asn Asp Asn Glu Thr Glu Pro Val Thr Val Ala Ser Ala Gly Gly Asp
 515 520 525

Leu His Met Thr Gln Phe Phe Arg Gly Asn Leu Ala Gly Leu Thr Leu
 530 535 540

Arg Ser Gly Lys Leu Ala Asp Lys Lys Val Ile Asp Cys Leu Tyr Thr
 545 550 555 560

Cys Lys Glu Gly Leu Asp Leu Gln Val Leu Glu Asp Ser Gly Arg Gly
 565 570 575

Val Gln Ile Gln Ala His Pro Ser Gln Leu Val Leu Thr Leu Glu Gly
 580 585 590

Glu Asp Leu Gly Glu Leu Asp Lys Ala Met Gln His Ile Ser Tyr Leu
 595 600 605

Asn Ser Arg Gln Phe Pro Thr Pro Gly Ile Arg Arg Leu Lys Ile Thr
 610 615 620

Ser Thr Ile Lys Cys Phe Asn Glu Ala Thr Cys Ile Ser Val Pro Pro
 625 630 635 640

Val Asp Gly Tyr Val Met Val Leu Gln Pro Glu Glu Pro Lys Ile Ser
 645 650 655

Protein Complexes associated with APP-processing

Leu Ser Gly Val His His Phe Ala Arg Ala Ala Ser Glu Phe Glu Ser
 660 665 670

Ser Glu Gly Val Phe Leu Phe Pro Glu Leu Arg Ile Ile Ser Thr Ile
 675 680 685

Thr Arg Glu Val Glu Pro Glu Gly Asp Gly Ala Glu Asp Pro Thr Val
 690 695 700

Gln Glu Ser Leu Val Ser Glu Glu Ile Val His Asp Leu Asp Thr Cys
 705 710 715 720

Glu Val Thr Val Glu Gly Glu Glu Leu Asn His Glu Gln Glu Ser Leu
 725 730 735

Glu Val Asp Met Ala Arg Leu Gln Gln Lys Gly Ile Glu Val Ser Ser
 740 745 750

Ser Glu Leu Gly Met Thr Phe Thr Gly Val Asp Thr Met Ala Ser Tyr
 755 760 765

Glu Glu Val Leu His Leu Leu Arg Tyr Arg Asn Trp His Ala Arg Ser
 770 775 780

Leu Leu Asp Arg Lys Phe Lys Leu Ile Cys Ser Glu Leu Asn Gly Arg
 785 790 795 800

Tyr Ile Ser Asn Glu Phe Lys Val Glu Val Asn Val Ile His Thr Ala
 805 810 815

Asn Pro Met Glu His Ala Asn His Met Ala Ala Gln Pro Gln Phe Val
 820 825 830

His Pro Glu His Arg Ser Phe Val Asp Leu Ser Gly His Asn Leu Ala
 835 840 845

Asn Pro His Pro Phe Ala Val Val Pro Ser Thr Ala Thr Val Val Ile
 850 855 860

Val Val Cys Val Ser Phe Leu Val Phe Met Ile Ile Leu Gly Val Phe
 865 870 875 880

Arg Ile Arg Ala Ala His Arg Arg Thr Met Arg Asp Gln Asp Thr Gly
 885 890 895

Lys Glu Asn Glu Met Asp Trp Asp Asp Ser Ala Leu Thr Ile Thr Val
 900 905 910

Asn Pro Met Glu Thr Tyr Glu Asp Gln His Ser Ser Glu Glu Glu Glu
 915 920 925

Protein Complexes associated with APP-processing
 Glu Glu Glu Glu Glu Glu Glu Ser Glu Asp Gly Glu Glu Glu Asp Asp
 930 935 940

Ile Thr Ser Ala Glu Ser Glu Ser Ser Glu Glu Glu Glu Gly Glu Gln
 945 950 955 960

Gly Asp Pro Gln Asn Ala Thr Arg Gln Gln Gln Leu Glu Trp Asp Asp
 965 970 975

Ser Thr Leu Ser Tyr
 980

<210> 48

<211> 955

<212> PRT

<213> Homo sapiens

<400> 48

Met Leu Pro Gly Arg Leu Cys Trp Val Pro Leu Leu Leu Ala Leu Gly
 1 5 10 15

Val Gly Ser Gly Ser Gly Gly Gly Gly Asp Ser Arg Gln Arg Arg Leu
 20 25 30

Leu Ala Ala Lys Val Asn Lys His Lys Pro Trp Ile Glu Thr Ser Tyr
 35 40 45

His Gly Val Ile Thr Glu Asn Asn Asp Thr Val Ile Leu Asp Pro Pro
 50 55 60

Leu Val Ala Leu Asp Lys Asp Ala Pro Val Pro Phe Ala Gly Glu Ile
 65 70 75 80

Cys Ala Phe Lys Ile His Gly Gln Glu Leu Pro Phe Glu Ala Val Val
 85 90 95

Leu Asn Lys Thr Ser Gly Glu Gly Arg Leu Arg Ala Lys Ser Pro Ile
 100 105 110

Asp Cys Glu Leu Gln Lys Glu Tyr Thr Phe Ile Ile Gln Ala Tyr Asp
 115 120 125

Cys Gly Ala Gly Pro His Glu Thr Ala Trp Lys Lys Ser His Lys Ala
 130 135 140

Val Val His Ile Gln Val Lys Asp Val Asn Glu Phe Ala Pro Thr Phe
 145 150 155 160

Protein Complexes associated with APP-processing

Lys Glu Pro Ala Tyr Lys Ala Val Val Thr Glu Gly Lys Ile Tyr Asp
165 170 175

Ser Ile Leu Gln Val Glu Ala Ile Asp Glu Asp Cys Ser Pro Gln Tyr
180 185 190

Ser Gln Ile Cys Asn Tyr Glu Ile Val Thr Thr Asp Val Pro Phe Ala
195 200 205

Ile Asp Arg Asn Gly Asn Ile Arg Asn Thr Glu Lys Leu Ser Tyr Asp
210 215 220

Lys Gln His Gln Tyr Glu Ile Leu Val Thr Ala Tyr Asp Cys Gly Gln
225 230 235 240

Lys Pro Ala Ala Gln Asp Thr Leu Val Gln Val Asp Val Lys Pro Val
245 250 255

Cys Lys Pro Gly Trp Gln Asp Trp Thr Lys Arg Ile Glu Tyr Gln Pro
260 265 270

Gly Ser Gly Ser Met Pro Leu Phe Pro Ser Ile His Leu Glu Thr Cys
275 280 285

Asp Gly Ala Val Ser Ser Leu Gln Ile Val Thr Glu Leu Gln Thr Asn
290 295 300

Tyr Ile Gly Lys Gly Cys Asp Arg Glu Thr Tyr Ser Glu Lys Ser Leu
305 310 315 320

Gln Lys Leu Cys Gly Ala Ser Ser Gly Ile Ile Asp Leu Leu Pro Ser
325 330 335

Pro Ser Ala Ala Thr Asn Trp Thr Ala Gly Leu Leu Val Asp Ser Ser
340 345 350

Glu Met Ile Phe Lys Phe Asp Gly Arg Gln Gly Ala Lys Ile Pro Asp
355 360 365

Gly Ile Val Pro Lys Asn Leu Thr Asp Gln Phe Thr Ile Thr Met Trp
370 375 380

Met Lys His Gly Pro Ser Pro Gly Val Arg Ala Glu Lys Glu Thr Ile
385 390 395 400

Leu Cys Asn Ser Asp Lys Thr Glu Met Asn Arg His His Tyr Ala Leu
405 410 415

Tyr Val His Asn Cys Arg Leu Val Phe Leu Leu Arg Lys Asp Phe Asp
420 425 430

Protein Complexes associated with APP-processing

Gln Ala Asp Thr Phe Arg Pro Ala Glu Phe His Trp Lys Leu Asp Gln
 435 440 445

Ile Cys Asp Lys Glu Trp His Tyr Tyr Val Ile Asn Val Glu Phe Pro
 450 455 460

Val Val Thr Leu Tyr Met Asp Gly Ala Thr Tyr Glu Pro Tyr Leu Val
 465 470 475 480

Thr Asn Asp Trp Pro Ile His Pro Ser His Ile Ala Met Gln Leu Thr
 485 490 495

Val Gly Ala Cys Trp Gln Gly Gly Glu Val Thr Lys Pro Gln Phe Ala
 500 505 510

Gln Phe Phe His Gly Ser Leu Ala Ser Leu Thr Ile Arg Pro Gly Lys
 515 520 525

Met Glu Ser Gln Lys Val Ile Ser Cys Leu Gln Ala Cys Lys Glu Gly
 530 535 540

Leu Asp Ile Asn Ser Leu Glu Ser Leu Gly Gln Gly Ile Lys Tyr His
 545 550 555 560

Phe Asn Pro Ser Gln Ser Ile Leu Val Met Glu Gly Asp Asp Ile Gly
 565 570 575

Asn Ile Asn Arg Ala Leu Gln Lys Val Ser Tyr Ile Asn Ser Arg Gln
 580 585 590

Phe Pro Thr Ala Gly Val Arg Arg Leu Lys Val Ser Ser Lys Val Gln
 595 600 605

Cys Phe Gly Glu Asp Val Cys Ile Ser Ile Pro Glu Val Asp Ala Tyr
 610 615 620

Val Met Val Leu Gln Ala Ile Glu Pro Arg Ile Thr Leu Arg Gly Thr
 625 630 635 640

Asp His Phe Trp Arg Pro Ala Ala Gln Phe Glu Ser Ala Arg Gly Val
 645 650 655

Thr Leu Phe Pro Asp Ile Lys Ile Val Ser Thr Phe Ala Lys Thr Glu
 660 665 670

Ala Pro Gly Asp Val Lys Thr Thr Asp Pro Lys Ser Glu Val Leu Glu
 675 680 685

Glu Met Leu His Asn Leu Asp Phe Cys Asp Ile Leu Val Ile Gly Gly
 690 695 700

Protein Complexes associated with APP-processing

Asp Leu Asp Pro Arg Gln Glu Cys Leu Glu Leu Asn His Ser Glu Leu
 705 710 715 720

His Gln Arg His Leu Asp Ala Thr Asn Ser Thr Ala Gly Tyr Ser Ile
 725 730 735

Tyr Gly Val Gly Ser Met Ser Arg Tyr Glu Gln Val Leu His His Ile
 740 745 750

Arg Tyr Arg Asn Trp Arg Pro Ala Ser Leu Glu Ala Arg Arg Phe Arg
 755 760 765

Ile Lys Cys Ser Glu Leu Asn Gly Arg Tyr Thr Ser Asn Glu Phe Asn
 770 775 780

Leu Glu Val Ser Ile Leu His Glu Asp Gln Val Ser Asp Lys Glu His
 785 790 795 800

Val Asn His Leu Ile Val Gln Pro Pro Phe Leu Gln Ser Val His His
 805 810 815

Pro Glu Ser Arg Ser Ser Ile Gln His Ser Ser Val Val Pro Ser Ile
 820 825 830

Ala Thr Val Val Ile Ile Ile Ser Val Cys Met Leu Val Phe Val Val
 835 840 845

Ala Met Gly Val Tyr Arg Val Arg Ile Ala His Gln His Phe Ile Gln
 850 855 860

Glu Thr Glu Ala Ala Lys Glu Ser Glu Met Asp Trp Asp Asp Ser Ala
 865 870 875 880

Leu Thr Ile Thr Val Asn Pro Met Glu Lys His Glu Gly Pro Gly His
 885 890 895

Gly Glu Asp Glu Thr Glu Gly Glu Glu Glu Glu Ala Glu Glu Glu
 900 905 910

Met Ser Ser Ser Ser Gly Ser Asp Asp Ser Glu Glu Glu Glu Glu Glu
 915 920 925

Glu Gly Met Gly Arg Gly Arg His Gly Gln Asn Gly Ala Arg Gln Ala
 930 935 940

Gln Leu Glu Trp Asp Asp Ser Thr Leu Pro Tyr
 945 950 955

<210> 49

<211> 956

<212> PRT Protein Complexes associated with APP-processing

<213> Homo sapiens

<400> 49

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Met Thr Leu Leu Leu Leu Pro Leu Leu Leu Ala Ser Leu Leu Ala Ser
1           5           10           15

Cys Ser Cys Asn Lys Ala Asn Lys His Lys Pro Trp Ile Glu Ala Glu
20           25           30

Tyr Gln Gly Ile Val Met Glu Asn Asp Asn Thr Val Leu Leu Asn Pro
35           40           45

Pro Leu Phe Ala Leu Asp Lys Asp Ala Pro Leu Arg Tyr Ala Gly Glu
50           55           60

Ile Cys Gly Phe Arg Leu His Gly Ser Gly Val Pro Phe Glu Ala Val
65           70           75           80

Ile Leu Asp Lys Ala Thr Gly Glu Gly Leu Ile Arg Ala Lys Glu Pro
85           90           95

Val Asp Cys Glu Ala Gln Lys Glu His Thr Phe Thr Ile Gln Ala Tyr
100          105          110

Asp Cys Gly Glu Gly Pro Asp Gly Ala Asn Thr Lys Lys Ser His Lys
115          120          125

Ala Thr Val His Val Arg Val Asn Asp Val Asn Glu Phe Ala Pro Val
130          135          140

Phe Val Glu Arg Leu Tyr Arg Ala Ala Val Thr Glu Gly Lys Leu Tyr
145          150          155          160

Asp Arg Ile Leu Arg Val Glu Ala Ile Asp Gly Asp Cys Ser Pro Gln
165          170          175

Tyr Ser Gln Ile Cys Tyr Tyr Glu Ile Leu Thr Pro Asn Thr Pro Phe
180          185          190

Leu Ile Asp Asn Asp Gly Asn Ile Glu Asn Thr Glu Lys Leu Gln Tyr
195          200          205

Ser Gly Glu Arg Leu Tyr Lys Phe Thr Val Thr Ala Tyr Asp Cys Gly
210          215          220

Lys Lys Arg Ala Ala Asp Asp Ala Glu Val Glu Ile Gln Val Lys Pro
225          230          235          240

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Protein Complexes associated with APP-processing

Thr Cys Lys Pro Ser Trp Gln Gly Trp Asn Lys Arg Ile Glu Tyr Ala
245 250 255

Pro Gly Ala Gly Ser Leu Ala Leu Phe Pro Gly Ile Arg Leu Glu Thr
260 265 270

Cys Asp Glu Pro Leu Trp Asn Ile Gln Ala Thr Ile Glu Leu Gln Thr
275 280 285

Ser His Val Ala Lys Gly Cys Asp Arg Asp Asn Tyr Ser Glu Arg Ala
290 295 300

Leu Arg Lys Leu Cys Gly Ala Ala Thr Gly Glu Val Asp Leu Leu Pro
305 310 315 320

Met Pro Gly Pro Asn Ala Asn Trp Thr Ala Gly Leu Ser Val His Tyr
325 330 335

Ser Gln Asp Ser Ser Leu Ile Tyr Trp Phe Asn Gly Thr Gln Ala Val
340 345 350

Gln Val Pro Leu Gly Gly Pro Ser Gly Leu Gly Ser Gly Pro Gln Asp
355 360 365

Ser Leu Ser Asp His Phe Thr Leu Ser Phe Trp Met Lys His Gly Val
370 375 380

Thr Pro Asn Lys Gly Lys Lys Glu Glu Glu Thr Ile Val Cys Asn Thr
385 390 395 400

Val Gln Asn Glu Asp Gly Phe Ser His Tyr Ser Leu Thr Val His Gly
405 410 415

Cys Arg Ile Ala Phe Leu Tyr Trp Pro Leu Leu Glu Ser Ala Arg Pro
420 425 430

Val Lys Phe Leu Trp Lys Leu Glu Gln Val Cys Asp Asp Glu Trp His
435 440 445

His Tyr Ala Leu Asn Leu Glu Phe Pro Thr Val Thr Leu Tyr Thr Asp
450 455 460

Gly Ile Ser Phe Asp Pro Ala Leu Ile His Asp Asn Gly Leu Ile His
465 470 475 480

Pro Pro Arg Arg Glu Pro Ala Leu Met Ile Gly Ala Cys Trp Thr Glu
485 490 495

Glu Lys Asn Lys Glu Lys Glu Lys Gly Asp Asn Ser Thr Asp Thr Thr
500 505 510

Protein Complexes associated with APP-processing

Gln Gly Asp Pro Leu Ser Ile His His Tyr Phe His Gly Tyr Leu Ala
 515 520 525

Gly Phe Ser Val Arg Ser Gly Arg Leu Glu Ser Arg Glu Val Ile Glu
 530 535 540

Cys Leu Tyr Ala Cys Arg Glu Gly Leu Asp Tyr Arg Asp Phe Glu Ser
 545 550 555 560

Leu Gly Lys Gly Met Lys Val His Val Asn Pro Ser Gln Ser Leu Leu
 565 570 575

Thr Leu Glu Gly Asp Asp Val Glu Thr Phe Asn His Ala Leu Gln His
 580 585 590

Val Ala Tyr Met Asn Thr Leu Arg Phe Ala Thr Pro Gly Val Arg Pro
 595 600 605

Leu Arg Leu Thr Thr Ala Val Lys Cys Phe Ser Glu Glu Ser Cys Val
 610 615 620

Ser Ile Pro Glu Val Glu Gly Tyr Val Val Val Leu Gln Pro Asp Ala
 625 630 635 640

Pro Gln Ile Leu Leu Ser Gly Thr Ala His Phe Ala Arg Pro Ala Val
 645 650 655

Asp Phe Glu Gly Thr Asn Gly Val Pro Leu Phe Pro Asp Leu Gln Ile
 660 665 670

Thr Cys Ser Ile Ser His Gln Val Glu Ala Lys Lys Asp Glu Ser Trp
 675 680 685

Gln Gly Thr Val Thr Asp Thr Arg Met Ser Asp Glu Ile Val His Asn
 690 695 700

Leu Asp Gly Cys Glu Ile Ser Leu Val Gly Asp Asp Leu Asp Pro Glu
 705 710 715 720

Arg Glu Ser Leu Leu Leu Asp Thr Thr Ser Leu Gln Gln Arg Gly Leu
 725 730 735

Glu Leu Thr Asn Thr Ser Ala Tyr Leu Thr Ile Ala Gly Val Glu Ser
 740 745 750

Ile Thr Val Tyr Glu Glu Ile Leu Arg Gln Ala Arg Tyr Arg Leu Arg
 755 760 765

His Gly Ala Ala Leu Tyr Thr Arg Lys Phe Arg Leu Ser Cys Ser Glu
 770 775 780

Protein Complexes associated with APP-processing
 Met Asn Gly Arg Tyr Ser Ser Asn Glu Phe Ile Val Glu Val Asn Val
 785 790 795 800

Leu His Ser Met Asn Arg Val Ala His Pro Ser His Val Leu Ser Ser
 805 810 815

Gln Gln Phe Leu His Arg Gly His Gln Pro Pro Pro Glu Met Ala Gly
 820 825 830

His Ser Leu Ala Ser Ser His Arg Asn Ser Met Ile Pro Ser Ala Ala
 835 840 845

Thr Leu Ile Ile Val Val Cys Val Gly Phe Leu Val Leu Met Val Val
 850 855 860

Leu Gly Leu Val Arg Ile His Ser Leu His Arg Arg Val Ser Gly Ala
 865 870 875 880

Gly Gly Pro Pro Gly Ala Ser Ser Asp Pro Lys Asp Pro Asp Leu Phe
 885 890 895

Trp Asp Asp Ser Ala Leu Thr Ile Ile Val Asn Pro Met Glu Ser Tyr
 900 905 910

Gln Asn Arg Gln Ser Cys Val Thr Gly Ala Val Gly Gly Gln Gln Glu
 915 920 925

Asp Glu Asp Ser Ser Asp Ser Glu Val Ala Asp Ser Pro Ser Ser Asp
 930 935 940

Glu Arg Arg Ile Ile Glu Thr Pro Pro His Arg Tyr
 945 950 955

<210> 50

<211> 1217

<212> PRT

<213> Homo sapiens

<400> 50

Met Tyr Ile Lys Gln Val Ile Ile Gln Gly Phe Arg Ser Tyr Arg Asp
 1 5 10 15

Gln Thr Ile Val Asp Pro Phe Ser Ser Lys His Asn Val Ile Val Gly
 20 25 30

Arg Asn Gly Ser Gly Lys Ser Asn Phe Phe Tyr Ala Ile Gln Phe Val
 35 40 45

Protein Complexes associated with APP-processing
 Leu Ser Asp Glu Phe Ser His Leu Arg Pro Glu Gln Arg Leu Ala Leu
 50 55 60

Leu His Glu Gly Thr Gly Pro Arg Val Ile Ser Ala Phe Val Glu Ile
 65 70 75 80

Ile Phe Asp Asn Ser Asp Asn Arg Leu Pro Ile Asp Lys Glu Glu Val
 85 90 95

Ser Leu Arg Arg Val Ile Gly Ala Lys Lys Asp Gln Tyr Phe Leu Asp
 100 105 110

Lys Lys Met Val Thr Lys Asn Asp Val Met Asn Leu Leu Glu Ser Ala
 115 120 125

Gly Phe Ser Arg Ser Asn Pro Tyr Tyr Ile Val Lys Gln Gly Lys Ile
 130 135 140

Asn Gln Met Ala Thr Ala Pro Asp Ser Gln Arg Leu Lys Leu Leu Arg
 145 150 155 160

Glu Val Ala Gly Thr Arg Val Tyr Asp Glu Arg Lys Glu Glu Ser Ile
 165 170 175

Ser Leu Met Lys Glu Thr Glu Gly Lys Arg Glu Lys Ile Asn Glu Leu
 180 185 190

Leu Lys Tyr Ile Glu Glu Arg Leu His Thr Leu Glu Glu Glu Lys Glu
 195 200 205

Glu Leu Ala Gln Tyr Gln Lys Trp Asp Lys Met Arg Arg Ala Leu Glu
 210 215 220

Tyr Thr Ile Tyr Asn Gln Glu Leu Asn Glu Thr Arg Ala Lys Leu Asp
 225 230 235 240

Glu Leu Ser Ala Lys Arg Glu Thr Ser Gly Glu Lys Ser Arg Gln Leu
 245 250 255

Arg Asp Ala Gln Gln Asp Ala Arg Asp Lys Met Glu Asp Ile Glu Arg
 260 265 270

Gln Val Arg Glu Leu Lys Thr Lys Ile Ser Ala Met Lys Glu Glu Lys
 275 280 285

Glu Gln Leu Ser Ala Glu Arg Gln Glu Gln Ile Lys Gln Arg Thr Lys
 290 295 300

Leu Glu Leu Lys Ala Lys Asp Leu Gln Asp Glu Leu Ala Gly Asn Ser
 305 310 315 320

Protein Complexes associated with APP-processing

Glu Gln Arg Lys Arg Leu Leu Lys Glu Arg Gln Lys Leu Leu Glu Lys
325 330 335

Ile Glu Glu Lys Gln Lys Glu Leu Ala Glu Thr Glu Pro Lys Phe Asn
340 345 350

Ser Val Lys Glu Lys Glu Glu Arg Gly Ile Ala Arg Leu Ala Gln Ala
355 360 365

Thr Gln Glu Arg Thr Asp Leu Tyr Ala Lys Gln Gly Arg Gly Ser Gln
370 375 380

Phe Thr Ser Lys Glu Glu Arg Asp Lys Trp Ile Lys Lys Glu Leu Lys
385 390 395 400

Ser Leu Asp Gln Ala Ile Asn Asp Lys Lys Arg Gln Ile Ala Ala Ile
405 410 415

His Lys Asp Leu Glu Asp Thr Glu Ala Asn Lys Glu Lys Asn Leu Glu
420 425 430

Gln Tyr Asn Lys Leu Asp Gln Asp Leu Asn Glu Val Lys Ala Arg Val
435 440 445

Glu Glu Leu Asp Arg Lys Tyr Tyr Glu Val Lys Asn Lys Lys Asp Glu
450 455 460

Leu Gln Ser Glu Arg Asn Tyr Leu Trp Arg Glu Glu Asn Ala Glu Gln
465 470 475 480

Gln Ala Leu Ala Ala Lys Arg Glu Asp Leu Glu Lys Lys Gln Gln Leu
485 490 495

Leu Arg Ala Ala Thr Gly Lys Ala Ile Leu Asn Gly Ile Asp Ser Ile
500 505 510

Asn Lys Val Leu Asp His Phe Arg Arg Lys Gly Ile Asn Gln His Val
515 520 525

Gln Asn Gly Tyr His Gly Ile Val Met Asn Asn Phe Glu Cys Glu Pro
530 535 540

Ala Phe Tyr Thr Cys Val Glu Val Thr Ala Gly Asn Arg Leu Phe Tyr
545 550 555 560

His Ile Val Asp Ser Asp Glu Val Ser Thr Lys Ile Leu Met Glu Phe
565 570 575

Asn Lys Met Asn Leu Pro Gly Glu Val Thr Phe Leu Pro Leu Asn Lys
580 585 590

Protein Complexes associated with APP-processing

Leu Asp Val Arg Asp Thr Ala Tyr Pro Glu Thr Asn Asp Ala Ile Pro
 595 600 605

Met Ile Ser Lys Leu Arg Tyr Asn Pro Arg Phe Asp Lys Ala Phe Lys
 610 615 620

His Val Phe Gly Lys Thr Leu Ile Cys Arg Ser Met Glu Val Ser Thr
 625 630 635 640

Gln Leu Ala Arg Ala Phe Thr Met Asp Cys Ile Thr Leu Glu Gly Asp
 645 650 655

Gln Val Ser His Arg Gly Ala Leu Thr Gly Gly Tyr Tyr Asp Thr Arg
 660 665 670

Lys Ser Arg Leu Glu Leu Gln Lys Asp Val Arg Lys Ala Glu Glu Glu
 675 680 685

Leu Gly Glu Leu Glu Ala Lys Leu Asn Glu Asn Leu Arg Arg Asn Ile
 690 695 700

Glu Arg Ile Asn Asn Glu Ile Asp Gln Leu Met Asn Gln Met Gln Gln
 705 710 715 720

Ile Glu Thr Gln Gln Arg Lys Phe Lys Ala Ser Arg Asp Ser Ile Leu
 725 730 735

Ser Glu Met Lys Met Leu Lys Glu Lys Arg Gln Gln Ser Glu Lys Thr
 740 745 750

Phe Met Pro Lys Gln Arg Ser Leu Gln Ser Leu Glu Ala Ser Leu His
 755 760 765

Ala Met Glu Ser Thr Arg Glu Ser Leu Lys Ala Glu Leu Gly Thr Asp
 770 775 780

Leu Leu Ser Gln Leu Ser Leu Glu Asp Gln Lys Arg Val Asp Ala Leu
 785 790 795 800

Asn Asp Glu Ile Arg Gln Leu Gln Gln Glu Asn Arg Gln Leu Leu Asn
 805 810 815

Glu Arg Ile Lys Leu Glu Gly Ile Ile Thr Arg Val Glu Thr Tyr Leu
 820 825 830

Asn Glu Asn Leu Arg Lys Arg Leu Asp Gln Val Glu Gln Glu Leu Asn
 835 840 845

Glu Leu Arg Glu Thr Glu Gly Gly Thr Val Leu Thr Ala Thr Thr Ser
 850 855 860

Protein Complexes associated with APP-processing

Glu Leu Glu Ala Ile Asn Lys Arg Val Lys Asp Thr Met Ala Arg Ser
 865 870 875 880

Glu Asp Leu Asp Asn Ser Ile Asp Lys Thr Glu Ala Gly Ile Lys Glu
 885 890 895

Leu Gln Lys Ser Met Glu Arg Trp Lys Asn Met Glu Lys Glu His Met
 900 905 910

Asp Ala Ile Asn His Asp Thr Lys Glu Leu Glu Lys Met Thr Asn Arg
 915 920 925

Gln Gly Met Leu Leu Lys Lys Lys Glu Glu Cys Met Lys Lys Ile Arg
 930 935 940

Glu Leu Gly Ser Leu Pro Gln Glu Ala Phe Glu Lys Tyr Gln Thr Leu
 945 950 955 960

Ser Leu Lys Gln Leu Phe Arg Lys Leu Glu Gln Cys Asn Thr Glu Leu
 965 970 975

Lys Lys Tyr Ser His Val Asn Lys Lys Ala Leu Asp Gln Phe Val Asn
 980 985 990

Phe Ser Glu Gln Lys Glu Lys Leu Ile Lys Arg Gln Glu Glu Leu Asp
 995 1000 1005

Arg Gly Tyr Lys Ser Ile Met Glu Leu Met Asn Val Leu Glu Leu
 1010 1015 1020

Arg Lys Tyr Glu Ala Ile Gln Leu Thr Phe Lys Gln Val Ser Lys
 1025 1030 1035

Asn Phe Ser Glu Val Phe Gln Lys Leu Val Pro Gly Gly Lys Ala
 1040 1045 1050

Thr Leu Val Met Lys Lys Gly Asp Val Glu Gly Ser Gln Ser Gln
 1055 1060 1065

Asp Glu Gly Glu Gly Ser Gly Glu Ser Glu Arg Gly Ser Gly Ser
 1070 1075 1080

Gln Ser Ser Val Pro Ser Val Asp Gln Phe Thr Gly Val Gly Ile
 1085 1090 1095

Arg Val Ser Phe Thr Gly Lys Gln Gly Glu Met Arg Glu Met Gln
 1100 1105 1110

Gln Leu Ser Gly Gly Gln Lys Ser Leu Val Ala Leu Ala Leu Ile
 1115 1120 1125

Protein Complexes associated with APP-processing

Phe Ala Ile Gln Lys Cys Asp Pro Ala Pro Phe Tyr Leu Phe Asp
 1130 1135 1140

Glu Ile Asp Gln Ala Leu Asp Ala Gln His Arg Lys Ala Val Ser
 1145 1150 1155

Asp Met Ile Met Glu Leu Ala Val His Ala Gln Phe Ile Thr Thr
 1160 1165 1170

Thr Phe Arg Pro Glu Leu Leu Glu Ser Ala Asp Lys Phe Tyr Gly
 1175 1180 1185

Val Lys Phe Arg Asn Lys Val Ser His Ile Asp Val Ile Thr Ala
 1190 1195 1200

Glu Met Ala Lys Asp Phe Val Glu Asp Asp Thr Thr His Gly
 1205 1210 1215

<210> 51
 <211> 1047
 <212> PRT
 <213> Homo sapiens

<400> 51

Met Ala Val Thr Leu Asp Lys Asp Ala Tyr Tyr Arg Arg Val Lys Arg
 1 5 10 15

Leu Tyr Ser Asn Trp Arg Lys Gly Glu Asp Glu Tyr Ala Asn Val Asp
 20 25 30

Ala Ile Val Val Ser Val Gly Val Asp Glu Glu Ile Val Tyr Ala Lys
 35 40 45

Ser Thr Ala Leu Gln Thr Trp Leu Phe Gly Tyr Glu Leu Thr Asp Thr
 50 55 60

Ile Met Val Phe Cys Asp Asp Lys Ile Ile Phe Met Ala Ser Lys Lys
 65 70 75 80

Lys Val Glu Phe Leu Lys Gln Ile Ala Asn Thr Lys Gly Asn Glu Asn
 85 90 95

Ala Asn Gly Ala Pro Ala Ile Thr Leu Leu Ile Arg Glu Lys Asn Glu
 100 105 110

Ser Asn Lys Ser Ser Phe Asp Lys Met Ile Glu Ala Ile Lys Glu Ser
 115 120 125

Protein Complexes associated with APP-processing

Lys Asn Gly Lys Lys Ile Gly Val Phe Ser Lys Asp Lys Phe Pro Gly
 130 135 140

Glu Phe Met Lys Ser Trp Asn Asp Cys Leu Asn Lys Glu Gly Phe Asp
 145 150 155 160

Lys Ile Asp Ile Ser Ala Val Val Ala Tyr Thr Ile Ala Val Lys Glu
 165 170 175

Asp Gly Glu Leu Asn Leu Met Lys Lys Ala Ala Ser Ile Thr Ser Glu
 180 185 190

Val Phe Asn Lys Phe Phe Lys Glu Arg Val Met Glu Ile Val Asp Ala
 195 200 205

Asp Glu Lys Val Arg His Ser Lys Leu Ala Glu Ser Val Glu Lys Ala
 210 215 220

Ile Glu Glu Lys Lys Tyr Leu Ala Gly Ala Asp Pro Ser Thr Val Glu
 225 230 235 240

Met Cys Tyr Pro Pro Ile Ile Gln Ser Gly Gly Asn Tyr Asn Leu Lys
 245 250 255

Phe Ser Val Val Ser Asp Lys Asn His Met His Phe Gly Ala Ile Thr
 260 265 270

Cys Ala Met Gly Ile Arg Phe Lys Ser Tyr Cys Ser Asn Leu Val Arg
 275 280 285

Thr Leu Met Val Asp Pro Ser Gln Glu Val Gln Glu Asn Tyr Asn Phe
 290 295 300

Leu Leu Gln Leu Gln Glu Glu Leu Leu Lys Glu Leu Arg His Gly Val
 305 310 315 320

Lys Ile Cys Asp Val Tyr Asn Ala Val Met Asp Val Val Lys Lys Gln
 325 330 335

Lys Pro Glu Leu Leu Asn Lys Ile Thr Lys Asn Leu Gly Phe Gly Met
 340 345 350

Gly Ile Glu Phe Arg Glu Gly Ser Leu Val Ile Asn Ser Lys Asn Gln
 355 360 365

Tyr Lys Leu Lys Lys Gly Met Val Phe Ser Ile Asn Leu Gly Phe Ser
 370 375 380

Asp Leu Thr Asn Lys Glu Gly Lys Lys Pro Glu Glu Lys Thr Tyr Ala
 385 390 395 400

Protein Complexes associated with APP-processing

Leu Phe Ile Gly Asp Thr Val Leu Val Asp Glu Asp Gly Pro Ala Thr
405 410 415

Val Leu Thr Ser Val Lys Lys Lys Val Lys Asn Val Gly Ile Phe Leu
420 425 430

Lys Asn Glu Asp Glu Glu Glu Glu Glu Glu Lys Asp Glu Ala Glu
435 440 445

Asp Leu Leu Gly Arg Gly Ser Arg Ala Ala Leu Leu Thr Glu Arg Thr
450 455 460

Arg Asn Glu Met Thr Ala Glu Glu Lys Arg Arg Ala His Gln Lys Glu
465 470 475 480

Leu Ala Ala Gln Leu Asn Glu Glu Ala Lys Arg Arg Leu Thr Glu Gln
485 490 495

Lys Gly Glu Gln Gln Ile Gln Lys Ala Arg Lys Ser Asn Val Ser Tyr
500 505 510

Lys Asn Pro Ser Leu Met Pro Lys Glu Pro His Ile Arg Glu Met Lys
515 520 525

Ile Tyr Ile Asp Lys Lys Tyr Glu Thr Val Ile Met Pro Val Phe Gly
530 535 540

Ile Ala Thr Pro Phe His Ile Ala Thr Ile Lys Asn Ile Ser Met Ser
545 550 555 560

Val Glu Gly Asp Tyr Thr Tyr Leu Arg Ile Asn Phe Tyr Cys Pro Gly
565 570 575

Ser Ala Leu Gly Arg Asn Glu Gly Asn Ile Phe Pro Asn Pro Glu Ala
580 585 590

Thr Phe Val Lys Glu Ile Thr Tyr Arg Ala Ser Asn Ile Lys Ala Pro
595 600 605

Gly Glu Gln Thr Val Pro Ala Leu Asn Leu Gln Asn Ala Phe Arg Ile
610 615 620

Ile Lys Glu Val Gln Lys Arg Tyr Lys Thr Arg Glu Ala Glu Glu Lys
625 630 635 640

Glu Lys Glu Gly Ile Val Lys Gln Asp Ser Leu Val Ile Asn Leu Asn
645 650 655

Arg Ser Asn Pro Lys Leu Lys Asp Leu Tyr Ile Arg Pro Asn Ile Ala
660 665 670

Protein Complexes associated with APP-processing

Gln Lys Arg Met Gln Gly Ser Leu Glu Ala His Val Asn Gly Phe Arg
675 680 685

Phe Thr Ser Val Arg Gly Asp Lys Val Asp Ile Leu Tyr Asn Asn Ile
690 695 700

Lys His Ala Leu Phe Gln Pro Cys Asp Gly Glu Met Ile Ile Val Leu
705 710 715 720

His Phe His Leu Lys Asn Ala Ile Met Phe Gly Lys Lys Arg His Thr
725 730 735

Asp Val Gln Phe Tyr Thr Glu Val Gly Glu Ile Thr Thr Asp Leu Gly
740 745 750

Lys His Gln His Met His Asp Arg Asp Asp Leu Tyr Ala Glu Gln Met
755 760 765

Glu Arg Glu Met Arg His Lys Leu Lys Thr Ala Phe Lys Asn Phe Ile
770 775 780

Glu Lys Val Glu Ala Leu Thr Lys Glu Glu Leu Glu Phe Glu Val Pro
785 790 795 800

Phe Arg Asp Leu Gly Phe Asn Gly Ala Pro Tyr Arg Ser Thr Cys Leu
805 810 815

Leu Gln Pro Thr Ser Ser Ala Leu Val Asn Ala Thr Glu Trp Pro Pro
820 825 830

Phe Val Val Thr Leu Asp Glu Val Glu Leu Ile His Phe Glu Arg Val
835 840 845

Gln Phe His Leu Lys Asn Phe Asp Met Val Ile Val Tyr Lys Asp Tyr
850 855 860

Ser Lys Lys Val Thr Met Ile Asn Ala Ile Pro Val Ala Ser Leu Asp
865 870 875 880

Pro Ile Lys Glu Trp Leu Asn Ser Cys Asp Leu Lys Tyr Thr Glu Gly
885 890 895

Val Gln Ser Leu Asn Trp Thr Lys Ile Met Lys Thr Ile Val Asp Asp
900 905 910

Pro Glu Gly Phe Phe Glu Gln Gly Gly Trp Ser Phe Leu Glu Pro Glu
915 920 925

Gly Glu Gly Ser Asp Ala Glu Glu Gly Asp Ser Glu Ser Glu Ile Glu
930 935 940

Protein Complexes associated with APP-processing

Asp Glu Thr Phe Asn Pro Ser Glu Asp Asp Tyr Glu Glu Glu Glu
 945 950 955 960

Asp Ser Asp Glu Asp Tyr Ser Ser Glu Ala Glu Glu Ser Asp Tyr Ser
 965 970 975

Lys Glu Ser Leu Gly Ser Glu Glu Glu Ser Gly Lys Asp Trp Asp Glu
 980 985 990

Leu Glu Glu Glu Ala Arg Lys Ala Asp Arg Glu Ser Arg Tyr Glu Glu
 995 1000 1005

Glu Glu Glu Gln Ser Arg Ser Met Ser Arg Lys Arg Lys Ala Ser
 1010 1015 1020

Val His Ser Ser Gly Arg Gly Ser Asn Arg Gly Ser Arg His Ser
 1025 1030 1035

Ser Ala Pro Pro Lys Lys Lys Arg Lys
 1040 1045

<210> 52
 <211> 101
 <212> PRT
 <213> Homo sapiens

<400> 52

Met Val Val Ser Lys Met Asn Lys Asp Ala Gln Met Arg Ala Ala Ile
 1 5 10 15

Asn Gln Lys Leu Ile Glu Thr Gly Glu Arg Glu Arg Leu Lys Glu Leu
 20 25 30

Leu Arg Ala Lys Leu Ile Glu Cys Gly Trp Lys Asp Gln Leu Lys Ala
 35 40 45

His Cys Lys Glu Val Ile Lys Glu Lys Gly Leu Glu His Val Thr Val
 50 55 60

Asp Asp Leu Val Ala Glu Ile Thr Pro Lys Gly Arg Ala Leu Val Pro
 65 70 75 80

Asp Ser Val Lys Lys Glu Leu Leu Gln Arg Ile Arg Thr Phe Leu Ala
 85 90 95

Gln His Ala Ser Leu
 100

Protein Complexes associated with APP-processing

<210> 53

<211> 96

<212> PRT

<213> Homo sapiens

<400> 53

Met Ala Glu Val Glu Glu Thr Leu Lys Arg Leu Gln Ser Gln Lys Gly
 1 5 10 15

Val Gln Gly Ile Ile Val Val Asn Thr Glu Gly Ile Pro Ile Lys Ser
 20 25 30

Thr Met Asp Asn Pro Thr Thr Thr Gln Tyr Ala Ser Leu Met His Ser
 35 40 45

Phe Ile Leu Lys Ala Arg Ser Thr Val Arg Asp Ile Asp Pro Gln Asn
 50 55 60

Asp Leu Thr Phe Leu Arg Ile Arg Ser Lys Lys Asn Glu Ile Met Val
 65 70 75 80

Ala Pro Asp Lys Asp Tyr Phe Leu Ile Val Ile Gln Asn Pro Thr Glu
 85 90 95

<210> 54

<211> 523

<212> PRT

<213> Homo sapiens

<400> 54

Met Ala Ala Val Gly Arg Val Gly Ser Phe Gly Ser Ser Pro Pro Gly
 1 5 10 15

Leu Ser Ser Thr Tyr Thr Gly Gly Pro Leu Gly Asn Glu Ile Ala Ser
 20 25 30

Gly Asn Gly Gly Ala Ala Ala Gly Asp Asp Glu Asp Gly Gln Asn Leu
 35 40 45

Trp Ser Cys Ile Leu Ser Glu Val Ser Thr Arg Ser Arg Ser Lys Leu
 50 55 60

Pro Ala Gly Lys Asn Val Leu Leu Leu Gly Glu Asp Gly Ala Gly Lys
 65 70 75 80

Protein Complexes associated with APP-processing

His Glu Asn Phe Gln Thr Leu Lys Ala Glu Asp Asn Phe Glu Asp Ile
340 345 350

Protein Complexes associated with APP-processing
 Ile Thr Lys Pro Pro Val Arg Lys Phe Val His Glu Lys Glu Ile Met
 355 360 365

Ala Glu Asp Asp Gln Val Phe Leu Met Lys Leu Gln Ser Leu Leu Ala
 370 375 380

Lys Gln Pro Pro Thr Ala Ala Gly Arg Pro Val Asp Ala Ser Pro Arg
 385 390 395 400

Val Pro Gly Gly Ser Pro Arg Thr Pro Asn Arg Ser Val Ser Ser Asn
 405 410 415

Val Ala Ser Val Ser Pro Ile Pro Ala Gly Ser Lys Lys Ile Asp Pro
 420 425 430

Asn Met Lys Ala Gly Ala Thr Ser Glu Gly Val Leu Ala Asn Phe Phe
 435 440 445

Asn Ser Leu Leu Ser Lys Lys Thr Gly Ser Pro Gly Gly Pro Gly Val
 450 455 460

Ser Gly Gly Ser Pro Ala Gly Gly Ala Gly Gly Gly Ser Ser Gly Leu
 465 470 475 480

Pro Pro Ser Thr Lys Lys Ser Gly Gln Lys Pro Val Leu Asp Val His
 485 490 495

Ala Glu Leu Asp Arg Ile Thr Arg Lys Pro Val Thr Val Ser Pro Thr
 500 505 510

Thr Pro Thr Ser Pro Thr Glu Gly Glu Ala Ser
 515 520

<210> 55

<211> 274

<212> PRT

<213> Homo sapiens

<400> 55

Met Val Cys Thr Cys Val Glu Gly Asp Asn Gln Phe Ile Val Thr Glu
 1 5 10 15

Ile Pro His Val Arg Gln Leu Ile Ser Gly Asp Gly Val Gly Glu Cys
 20 25 30

Ala Val Arg Ala Ala Thr Glu Gly Arg Thr Leu Ile Leu Glu Gly Leu
 35 40 45

Protein Complexes associated with APP-processing

Glu Lys Ala Glu Arg Asn Val Leu Pro Val Leu Asn Asn Leu Leu Glu
 50 55 60

Asn Arg Glu Met Gln Leu Glu Asp Gly Arg Phe Leu Met Ser Ala Glu
 65 70 75 80

Arg Tyr Asp Lys Leu Leu Arg Asp His Thr Lys Lys Glu Leu Asp Ser
 85 90 95

Trp Lys Ile Val Arg Val Ser Glu Asn Phe Arg Val Ile Ala Leu Gly
 100 105 110

Leu Pro Val Pro Arg Tyr Ser Gly Asn Pro Leu Asp Pro Pro Leu Arg
 115 120 125

Ser Arg Phe Gln Ala Arg Asp Ile Tyr Tyr Leu Pro Phe Lys Asp Gln
 130 135 140

Leu Lys Leu Leu Tyr Ser Ile Gly Ala Asn Val Ser Ala Glu Lys Val
 145 150 155 160

Ser Gln Leu Leu Ser Phe Ala Thr Thr Leu Cys Ser Gln Glu Ser Ser
 165 170 175

Thr Leu Gly Leu Pro Asp Phe Pro Leu Asp Ser Leu Ala Ala Ala Val
 180 185 190

Gln Ile Leu Asp Ser Phe Pro Met Met Pro Ile Lys His Ala Ile Gln
 195 200 205

Trp Leu Tyr Pro Tyr Ser Ile Leu Leu Gly His Glu Gly Lys Met Ala
 210 215 220

Val Glu Gly Val Leu Lys Arg Phe Glu Leu Gln Asp Ser Gly Ser Ser
 225 230 235 240

Leu Leu Pro Lys Glu Ile Val Lys Val Glu Lys Met Met Glu Asn His
 245 250 255

Val Ser Gln Ala Ser Val Thr Ile Arg Ile Ala Asp Lys Glu Val Thr
 260 265 270

Ile Lys

<210> 56

<211> 406

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 56

Met Ser Ala Ser Gln Asp Ser Arg Ser Arg Asp Asn Gly Pro Asp Gly
 1 5 10 15

Met Glu Pro Glu Gly Val Ile Glu Ser Asn Trp Asn Glu Ile Val Asp
 20 25 30

Ser Phe Asp Asp Met Asn Leu Ser Glu Ser Leu Leu Arg Gly Ile Tyr
 35 40 45

Ala Tyr Gly Phe Glu Lys Pro Ser Ala Ile Gln Gln Arg Ala Ile Leu
 50 55 60

Pro Cys Ile Lys Gly Tyr Asp Val Ile Ala Gln Ala Gln Ser Gly Thr
 65 70 75 80

Gly Lys Thr Ala Thr Phe Ala Ile Ser Ile Leu Gln Gln Ile Glu Leu
 85 90 95

Asp Leu Lys Ala Thr Gln Ala Leu Val Leu Ala Pro Thr Arg Glu Leu
 100 105 110

Ala Gln Gln Ile Gln Lys Val Val Met Ala Leu Gly Asp Tyr Met Gly
 115 120 125

Ala Ser Cys His Ala Cys Ile Gly Gly Thr Asn Val Arg Ala Glu Val
 130 135 140

Gln Lys Leu Gln Met Glu Ala Pro His Ile Ile Val Gly Thr Pro Gly
 145 150 155 160

Arg Val Phe Asp Met Leu Asn Arg Arg Tyr Leu Ser Pro Lys Tyr Ile
 165 170 175

Lys Met Phe Val Leu Asp Glu Ala Asp Glu Met Leu Ser Arg Gly Phe
 180 185 190

Lys Asp Gln Ile Tyr Asp Ile Phe Gln Lys Leu Asn Ser Asn Thr Gln
 195 200 205

Val Val Leu Leu Ser Ala Thr Met Pro Ser Asp Val Leu Glu Val Thr
 210 215 220

Lys Lys Phe Met Arg Asp Pro Ile Arg Ile Leu Val Lys Lys Glu Glu
 225 230 235 240

Leu Thr Leu Glu Gly Ile Arg Gln Phe Tyr Ile Asn Val Glu Arg Glu
 245 250 255

Protein Complexes associated with APP-processing

Glu Trp Lys Leu Asp Thr Leu Cys Asp Leu Tyr Glu Thr Leu Thr Ile
 260 265 270

Thr Gln Ala Val Ile Phe Ile Asn Thr Arg Arg Lys Val Asp Trp Leu
 275 280 285

Thr Glu Lys Met His Ala Arg Asp Phe Thr Val Ser Ala Met His Gly
 290 295 300

Asp Met Asp Gln Lys Glu Arg Asp Val Ile Met Arg Glu Phe Arg Ser
 305 310 315 320

Gly Ser Ser Arg Val Leu Ile Thr Thr Asp Leu Leu Ala Arg Gly Ile
 325 330 335

Asp Val Gln Gln Val Ser Leu Val Ile Asn Tyr Asp Leu Pro Thr Asn
 340 345 350

Arg Glu Asn Tyr Ile His Arg Ile Gly Arg Gly Gly Arg Phe Gly Arg
 355 360 365

Lys Gly Val Ala Ile Asn Met Val Thr Glu Glu Asp Lys Arg Thr Leu
 370 375 380

Arg Asp Ile Glu Thr Phe Tyr Asn Thr Ser Ile Glu Glu Met Pro Leu
 385 390 395 400

Asn Val Ala Asp Leu Ile
 405

<210> 57

<211> 391

<212> PRT

<213> Homo sapiens

<400> 57

Met Asp Gln Cys Val Thr Val Glu Arg Glu Leu Glu Lys Val Leu His
 1 5 10 15

Lys Phe Ser Gly Tyr Gly Gln Leu Cys Glu Arg Gly Leu Glu Glu Leu
 20 25 30

Ile Asp Tyr Thr Gly Gly Leu Lys His Glu Ile Leu Gln Ser His Gly
 35 40 45

Gln Asp Ala Glu Leu Ser Gly Thr Leu Ser Leu Val Leu Thr Gln Cys
 50 55 60

Protein Complexes associated with APP-processing

Cys Lys Arg Ile Lys Asp Thr Val Gln Lys Leu Ala Ser Asp His Lys
 65 70 75 80

Asp Ile His Ser Ser Val Ser Arg Val Gly Lys Ala Ile Asp Lys Asn
 85 90 95

Phe Asp Ser Asp Ile Ser Ser Val Gly Ile Asp Gly Cys Trp Gln Ala
 100 105 110

Asp Ser Gln Arg Leu Leu Asn Glu Val Met Val Glu His Phe Phe Arg
 115 120 125

Gln Gly Met Leu Asp Val Ala Glu Glu Leu Cys Gln Glu Ser Gly Leu
 130 135 140

Ser Val Asp Pro Ser Gln Lys Glu Pro Phe Val Glu Leu Asn Arg Ile
 145 150 155 160

Leu Glu Ala Leu Lys Val Arg Val Leu Arg Pro Ala Leu Glu Trp Ala
 165 170 175

Val Ser Asn Arg Glu Met Leu Ile Ala Gln Asn Ser Ser Leu Glu Phe
 180 185 190

Lys Leu His Arg Leu Tyr Phe Ile Ser Leu Leu Met Gly Gly Thr Thr
 195 200 205

Asn Gln Arg Glu Ala Leu Gln Tyr Ala Lys Asn Phe Gln Pro Phe Ala
 210 215 220

Leu Asn His Gln Lys Asp Ile Gln Val Leu Met Gly Ser Leu Val Tyr
 225 230 235 240

Leu Arg Gln Gly Ile Glu Asn Ser Pro Tyr Val His Leu Leu Asp Ala
 245 250 255

Asn Gln Trp Ala Asp Ile Cys Asp Ile Phe Thr Arg Asp Ala Cys Ala
 260 265 270

Leu Leu Gly Leu Ser Val Glu Ser Pro Leu Ser Val Ser Phe Ser Ala
 275 280 285

Gly Cys Val Ala Leu Pro Ala Leu Ile Asn Ile Lys Ala Val Ile Glu
 290 295 300

Gln Arg Gln Cys Thr Gly Val Trp Asn Gln Lys Asp Glu Leu Pro Ile
 305 310 315 320

Glu Val Asp Leu Gly Lys Lys Cys Trp Tyr His Ser Ile Phe Ala Cys
 325 330 335

Protein Complexes associated with APP-processing
 Pro Ile Leu Arg Gln Gln Thr Thr Asp Asn Asn Pro Pro Met Lys Leu
 340 345 350

Val Cys Gly His Ile Ile Ser Arg Asp Ala Leu Asn Lys Met Phe Asn
 355 360 365

Gly Ser Lys Leu Lys Cys Pro Tyr Cys Pro Met Glu Gln Ser Pro Gly
 370 375 380

Asp Ala Lys Gln Ile Phe Phe
 385 390

<210> 58

<211> 2549

<212> PRT

<213> Homo sapiens

<400> 58

Met Leu Gly Thr Gly Pro Ala Ala Ala Thr Thr Ala Ala Thr Thr Ser
 1 5 10 15

Ser Asn Val Ser Val Leu Gln Gln Phe Ala Ser Gly Leu Lys Ser Arg
 20 25 30

Asn Glu Glu Thr Arg Ala Lys Ala Ala Lys Glu Leu Gln His Tyr Val
 35 40 45

Thr Met Glu Leu Arg Glu Met Ser Gln Glu Glu Ser Thr Arg Phe Tyr
 50 55 60

Asp Gln Leu Asn His His Ile Phe Glu Leu Val Ser Ser Ser Asp Ala
 65 70 75 80

Asn Glu Arg Lys Gly Gly Ile Leu Ala Ile Ala Ser Leu Ile Gly Val
 85 90 95

Glu Gly Gly Asn Ala Thr Arg Ile Gly Arg Phe Ala Asn Tyr Leu Arg
 100 105 110

Asn Leu Leu Pro Ser Asn Asp Pro Val Val Met Glu Met Ala Ser Lys
 115 120 125

Ala Ile Gly Arg Leu Ala Met Ala Gly Asp Thr Phe Thr Ala Glu Tyr
 130 135 140

Val Glu Phe Glu Val Lys Arg Ala Leu Glu Trp Leu Gly Ala Asp Arg
 145 150 155 160

Protein Complexes associated with APP-processing

Asn Glu Gly Arg Arg His Ala Ala Val Leu Val Leu Arg Glu Leu Ala
165 170 175

Ile Ser Val Pro Thr Phe Phe Phe Gln Gln Val Gln Pro Phe Phe Asp
180 185 190

Asn Ile Phe Val Ala Val Trp Asp Pro Lys Gln Ala Ile Arg Glu Gly
195 200 205

Ala Val Ala Ala Leu Arg Ala Cys Leu Ile Leu Thr Thr Gln Arg Glu
210 215 220

Pro Lys Glu Met Gln Lys Pro Gln Trp Tyr Arg His Thr Phe Glu Glu
225 230 235 240

Ala Glu Lys Gly Phe Asp Glu Thr Leu Ala Lys Glu Lys Gly Met Asn
245 250 255

Arg Asp Asp Arg Ile His Gly Ala Leu Leu Ile Leu Asn Glu Leu Val
260 265 270

Arg Ile Ser Ser Met Glu Gly Glu Arg Leu Arg Glu Glu Met Glu Glu
275 280 285

Ile Thr Gln Gln Gln Leu Val His Asp Lys Tyr Cys Lys Asp Leu Met
290 295 300

Gly Phe Gly Thr Lys Pro Arg His Ile Thr Pro Phe Thr Ser Phe Gln
305 310 315 320

Ala Val Gln Pro Gln Gln Ser Asn Ala Leu Val Gly Leu Leu Gly Tyr
325 330 335

Ser Ser His Gln Gly Leu Met Gly Phe Gly Thr Ser Pro Ser Pro Ala
340 345 350

Lys Ser Thr Leu Val Glu Ser Arg Cys Cys Arg Asp Leu Met Glu Glu
355 360 365

Lys Phe Asp Gln Val Cys Gln Trp Val Leu Lys Cys Arg Asn Ser Lys
370 375 380

Asn Ser Leu Ile Gln Met Thr Ile Leu Asn Leu Leu Pro Arg Leu Ala
385 390 395 400

Ala Phe Arg Pro Ser Ala Phe Thr Asp Thr Gln Tyr Leu Gln Asp Thr
405 410 415

Met Asn His Val Leu Ser Cys Val Lys Lys Glu Lys Glu Arg Thr Ala
420 425 430

Protein Complexes associated with APP-processing

Ala Phe Gln Ala Leu Gly Leu Leu Ser Val Ala Val Arg Ser Glu Phe
 435 440 445

Lys Val Tyr Leu Pro Arg Val Leu Asp Ile Ile Arg Ala Ala Leu Pro
 450 455 460

Pro Lys Asp Phe Ala His Lys Arg Gln Lys Ala Met Gln Val Asp Ala
 465 470 475 480

Thr Val Phe Thr Cys Ile Ser Met Leu Ala Arg Ala Met Gly Pro Gly
 485 490 495

Ile Gln Gln Asp Ile Lys Glu Leu Leu Glu Pro Met Leu Ala Val Gly
 500 505 510

Leu Ser Pro Ala Leu Thr Ala Val Leu Tyr Asp Leu Ser Arg Gln Ile
 515 520 525

Pro Gln Leu Lys Lys Asp Ile Gln Asp Gly Leu Leu Lys Met Leu Ser
 530 535 540

Leu Val Leu Met His Lys Pro Leu Arg His Pro Gly Met Pro Lys Gly
 545 550 555 560

Leu Ala His Gln Leu Ala Ser Pro Gly Leu Thr Thr Leu Pro Glu Ala
 565 570 575

Ser Asp Val Gly Ser Ile Thr Leu Ala Leu Arg Thr Leu Gly Ser Phe
 580 585 590

Glu Phe Glu Gly His Ser Leu Thr Gln Phe Val Arg His Cys Ala Asp
 595 600 605

His Phe Leu Asn Ser Glu His Lys Glu Ile Arg Met Glu Ala Ala Arg
 610 615 620

Thr Cys Ser Arg Leu Leu Thr Pro Ser Ile His Leu Ile Ser Gly His
 625 630 635 640

Ala His Val Val Ser Gln Thr Ala Val Gln Val Val Ala Asp Val Leu
 645 650 655

Ser Lys Leu Leu Val Val Gly Ile Thr Asp Pro Asp Pro Asp Ile Arg
 660 665 670

Tyr Cys Val Leu Ala Ser Leu Asp Glu Arg Phe Asp Ala His Leu Ala
 675 680 685

Gln Ala Glu Asn Leu Gln Ala Leu Phe Val Ala Leu Asn Asp Gln Val
 690 695 700

Protein Complexes associated with APP-processing
 Phe Glu Ile Arg Glu Leu Ala Ile Cys Thr Val Gly Arg Leu Ser Ser
 705 710 715 720

Met Asn Pro Ala Phe Val Met Pro Phe Leu Arg Lys Met Leu Ile Gln
 725 730 735

Ile Leu Thr Glu Leu Glu His Ser Gly Ile Gly Arg Ile Lys Glu Gln
 740 745 750

Ser Ala Arg Met Leu Gly His Leu Val Ser Asn Ala Pro Arg Leu Ile
 755 760 765

Arg Pro Tyr Met Glu Pro Ile Leu Lys Ala Leu Ile Leu Lys Leu Lys
 770 775 780

Asp Pro Asp Pro Asp Pro Asn Pro Gly Val Ile Asn Asn Val Leu Ala
 785 790 795 800

Thr Ile Gly Glu Leu Ala Gln Val Ser Gly Leu Glu Met Arg Lys Trp
 805 810 815

Val Asp Glu Leu Phe Ile Ile Ile Met Asp Met Leu Gln Asp Ser Ser
 820 825 830

Leu Leu Ala Lys Arg Gln Val Ala Leu Trp Thr Leu Gly Gln Leu Val
 835 840 845

Ala Ser Thr Gly Tyr Val Val Glu Pro Tyr Arg Lys Tyr Pro Thr Leu
 850 855 860

Leu Glu Val Leu Leu Asn Phe Leu Lys Thr Glu Gln Asn Gln Gly Thr
 865 870 875 880

Arg Arg Glu Ala Ile Arg Val Leu Gly Leu Leu Gly Ala Leu Asp Pro
 885 890 895

Tyr Lys His Lys Val Asn Ile Gly Met Ile Asp Gln Ser Arg Asp Ala
 900 905 910

Ser Ala Val Ser Leu Ser Glu Ser Lys Ser Ser Gln Asp Ser Ser Asp
 915 920 925

Tyr Ser Thr Ser Glu Met Leu Val Asn Met Gly Asn Leu Pro Leu Asp
 930 935 940

Glu Phe Tyr Pro Ala Val Ser Met Val Ala Leu Met Arg Ile Phe Arg
 945 950 955 960

Asp Gln Ser Leu Ser His His His Thr Met Val Val Gln Ala Ile Thr
 965 970 975

Protein Complexes associated with APP-processing

Gly Tyr Thr Leu Ala Asp Glu Glu Glu Asp Pro Leu Ile Tyr Gln
1220 1225 1230

Protein Complexes associated with APP-processing

His	Arg	Met	Leu	Arg	Ser	Gly	Gln	Gly	Asp	Ala	Leu	Ala	Ser	Gly
	1235					1240					1245			
Pro	Val	Glu	Thr	Gly	Pro	Met	Lys	Lys	Leu	His	Val	Ser	Thr	Ile
	1250					1255					1260			
Asn	Leu	Gln	Lys	Ala	Trp	Gly	Ala	Ala	Arg	Arg	Val	Ser	Lys	Asp
	1265					1270					1275			
Asp	Trp	Leu	Glu	Trp	Leu	Arg	Arg	Leu	Ser	Leu	Glu	Leu	Leu	Lys
	1280					1285					1290			
Asp	Ser	Ser	Ser	Pro	Ser	Leu	Arg	Ser	Cys	Trp	Ala	Leu	Ala	Gln
	1295					1300					1305			
Ala	Tyr	Asn	Pro	Met	Ala	Arg	Asp	Leu	Phe	Asn	Ala	Ala	Phe	Val
	1310					1315					1320			
Ser	Cys	Trp	Ser	Glu	Leu	Asn	Glu	Asp	Gln	Gln	Asp	Glu	Leu	Ile
	1325					1330					1335			
Arg	Ser	Ile	Glu	Leu	Ala	Leu	Thr	Ser	Gln	Asp	Ile	Ala	Glu	Val
	1340					1345					1350			
Thr	Gln	Thr	Leu	Leu	Asn	Leu	Ala	Glu	Phe	Met	Glu	His	Ser	Asp
	1355					1360					1365			
Lys	Gly	Pro	Leu	Pro	Leu	Arg	Asp	Asp	Asn	Gly	Ile	Val	Leu	Leu
	1370					1375					1380			
Gly	Glu	Arg	Ala	Ala	Lys	Cys	Arg	Ala	Tyr	Ala	Lys	Ala	Leu	His
	1385					1390					1395			
Tyr	Lys	Glu	Leu	Glu	Phe	Gln	Lys	Gly	Pro	Thr	Pro	Ala	Ile	Leu
	1400					1405					1410			
Glu	Ser	Leu	Ile	Ser	Ile	Asn	Asn	Lys	Leu	Gln	Gln	Pro	Glu	Ala
	1415					1420					1425			
Ala	Ala	Gly	Val	Leu	Glu	Tyr	Ala	Met	Lys	His	Phe	Gly	Glu	Leu
	1430					1435					1440			
Glu	Ile	Gln	Ala	Thr	Trp	Tyr	Glu	Lys	Leu	His	Glu	Trp	Glu	Asp
	1445					1450					1455			
Ala	Leu	Val	Ala	Tyr	Asp	Lys	Lys	Met	Asp	Thr	Asn	Lys	Asp	Asp
	1460					1465					1470			
Pro	Glu	Leu	Met	Leu	Gly	Arg	Met	Arg	Cys	Leu	Glu	Ala	Leu	Gly
	1475					1480					1485			

Protein Complexes associated with APP-processing

Glu	Trp	Gly	Gln	Leu	His	Gln	Gln	Cys	Cys	Glu	Lys	Trp	Thr	Leu
1490						1495					1500			
Val	Asn	Asp	Glu	Thr	Gln	Ala	Lys	Met	Ala	Arg	Met	Ala	Ala	Ala
1505						1510					1515			
Ala	Ala	Trp	Gly	Leu	Gly	Gln	Trp	Asp	Ser	Met	Glu	Glu	Tyr	Thr
1520						1525					1530			
Cys	Met	Ile	Pro	Arg	Asp	Thr	His	Asp	Gly	Ala	Phe	Tyr	Arg	Ala
1535						1540					1545			
Val	Leu	Ala	Leu	His	Gln	Asp	Leu	Phe	Ser	Leu	Ala	Gln	Gln	Cys
1550						1555					1560			
Ile	Asp	Lys	Ala	Arg	Asp	Leu	Leu	Asp	Ala	Glu	Leu	Thr	Ala	Met
1565						1570					1575			
Ala	Gly	Glu	Ser	Tyr	Ser	Arg	Ala	Tyr	Gly	Ala	Met	Val	Ser	Cys
1580						1585					1590			
His	Met	Leu	Ser	Glu	Leu	Glu	Glu	Val	Ile	Gln	Tyr	Lys	Leu	Val
1595						1600					1605			
Pro	Glu	Arg	Arg	Glu	Ile	Ile	Arg	Gln	Ile	Trp	Trp	Glu	Arg	Leu
1610						1615					1620			
Gln	Gly	Cys	Gln	Arg	Ile	Val	Glu	Asp	Trp	Gln	Lys	Ile	Leu	Met
1625						1630					1635			
Val	Arg	Ser	Leu	Val	Val	Ser	Pro	His	Glu	Asp	Met	Arg	Thr	Trp
1640						1645					1650			
Leu	Lys	Tyr	Ala	Ser	Leu	Cys	Gly	Lys	Ser	Gly	Arg	Leu	Ala	Leu
1655						1660					1665			
Ala	His	Lys	Thr	Leu	Val	Leu	Leu	Leu	Gly	Val	Asp	Pro	Ser	Arg
1670						1675					1680			
Gln	Leu	Asp	His	Pro	Leu	Pro	Thr	Val	His	Pro	Gln	Val	Thr	Tyr
1685						1690					1695			
Ala	Tyr	Met	Lys	Asn	Met	Trp	Lys	Ser	Ala	Arg	Lys	Ile	Asp	Ala
1700						1705					1710			
Phe	Gln	His	Met	Gln	His	Phe	Val	Gln	Thr	Met	Gln	Gln	Gln	Ala
1715						1720					1725			
Gln	His	Ala	Ile	Ala	Thr	Glu	Asp	Gln	Gln	His	Lys	Gln	Glu	Leu
1730						1735					1740			

Protein Complexes associated with APP-processing

His	Lys	Leu	Met	Ala	Arg	Cys	Phe	Leu	Lys	Leu	Gly	Glu	Trp	Gln
	1745					1750					1755			
Leu	Asn	Leu	Gln	Gly	Ile	Asn	Glu	Ser	Thr	Ile	Pro	Lys	Val	Leu
	1760					1765					1770			
Gln	Tyr	Tyr	Ser	Ala	Ala	Thr	Glu	His	Asp	Arg	Ser	Trp	Tyr	Lys
	1775					1780					1785			
Ala	Trp	His	Ala	Trp	Ala	Val	Met	Asn	Phe	Glu	Ala	Val	Leu	His
	1790					1795					1800			
Tyr	Lys	His	Gln	Asn	Gln	Ala	Arg	Asp	Glu	Lys	Lys	Lys	Leu	Arg
	1805					1810					1815			
His	Ala	Ser	Gly	Ala	Asn	Ile	Thr	Asn	Ala	Thr	Thr	Ala	Ala	Thr
	1820					1825					1830			
Thr	Ala	Ala	Thr	Ala	Thr	Thr	Thr	Ala	Ser	Thr	Glu	Gly	Ser	Asn
	1835					1840					1845			
Ser	Glu	Ser	Glu	Ala	Glu	Ser	Thr	Glu	Asn	Ser	Pro	Thr	Pro	Ser
	1850					1855					1860			
Pro	Leu	Gln	Lys	Lys	Val	Thr	Glu	Asp	Leu	Ser	Lys	Thr	Leu	Leu
	1865					1870					1875			
Met	Tyr	Thr	Val	Pro	Ala	Val	Gln	Gly	Phe	Phe	Arg	Ser	Ile	Ser
	1880					1885					1890			
Leu	Ser	Arg	Gly	Asn	Asn	Leu	Gln	Asp	Thr	Leu	Arg	Val	Leu	Thr
	1895					1900					1905			
Leu	Trp	Phe	Asp	Tyr	Gly	His	Trp	Pro	Asp	Val	Asn	Glu	Ala	Leu
	1910					1915					1920			
Val	Glu	Gly	Val	Lys	Ala	Ile	Gln	Ile	Asp	Thr	Trp	Leu	Gln	Val
	1925					1930					1935			
Ile	Pro	Gln	Leu	Ile	Ala	Arg	Ile	Asp	Thr	Pro	Arg	Pro	Leu	Val
	1940					1945					1950			
Gly	Arg	Leu	Ile	His	Gln	Leu	Leu	Thr	Asp	Ile	Gly	Arg	Tyr	His
	1955					1960					1965			
Pro	Gln	Ala	Leu	Ile	Tyr	Pro	Leu	Thr	Val	Ala	Ser	Lys	Ser	Thr
	1970					1975					1980			
Thr	Thr	Ala	Arg	His	Asn	Ala	Ala	Asn	Lys	Ile	Leu	Lys	Asn	Met
	1985					1990					1995			

Protein Complexes associated with APP-processing

Cys	Glu	His	Ser	Asn	Thr	Leu	Val	Gln	Gln	Ala	Met	Met	Val	Ser
2000						2005					2010			
Glu	Glu	Leu	Ile	Arg	Val	Ala	Ile	Leu	Trp	His	Glu	Met	Trp	His
2015						2020					2025			
Glu	Gly	Leu	Glu	Glu	Ala	Ser	Arg	Leu	Tyr	Phe	Gly	Glu	Arg	Asn
2030						2035					2040			
Val	Lys	Gly	Met	Phe	Glu	Val	Leu	Glu	Pro	Leu	His	Ala	Met	Met
2045						2050					2055			
Glu	Arg	Gly	Pro	Gln	Thr	Leu	Lys	Glu	Thr	Ser	Phe	Asn	Gln	Ala
2060						2065					2070			
Tyr	Gly	Arg	Asp	Leu	Met	Glu	Ala	Gln	Glu	Trp	Cys	Arg	Lys	Tyr
2075						2080					2085			
Met	Lys	Ser	Gly	Asn	Val	Lys	Asp	Leu	Thr	Gln	Ala	Trp	Asp	Leu
2090						2095					2100			
Tyr	Tyr	His	Val	Phe	Arg	Arg	Ile	Ser	Lys	Gln	Leu	Pro	Gln	Leu
2105						2110					2115			
Thr	Ser	Leu	Glu	Leu	Gln	Tyr	Val	Ser	Pro	Lys	Leu	Leu	Met	Cys
2120						2125					2130			
Arg	Asp	Leu	Glu	Leu	Ala	Val	Pro	Gly	Thr	Tyr	Asp	Pro	Asn	Gln
2135						2140					2145			
Pro	Ile	Ile	Arg	Ile	Gln	Ser	Ile	Ala	Pro	Ser	Leu	Gln	Val	Ile
2150						2155					2160			
Thr	Ser	Lys	Gln	Arg	Pro	Arg	Lys	Leu	Thr	Leu	Met	Gly	Ser	Asn
2165						2170					2175			
Gly	His	Glu	Phe	Val	Phe	Leu	Leu	Lys	Gly	His	Glu	Asp	Leu	Arg
2180						2185					2190			
Gln	Asp	Glu	Arg	Val	Met	Gln	Leu	Phe	Gly	Leu	Val	Asn	Thr	Leu
2195						2200					2205			
Leu	Ala	Asn	Asp	Pro	Thr	Ser	Leu	Arg	Lys	Asn	Leu	Ser	Ile	Gln
2210						2215					2220			
Arg	Tyr	Ala	Val	Ile	Pro	Leu	Ser	Thr	Asn	Ser	Gly	Leu	Ile	Gly
2225						2230					2235			
Trp	Val	Pro	His	Cys	Asp	Thr	Leu	His	Ala	Leu	Ile	Arg	Asp	Tyr
2240						2245					2250			

Protein Complexes associated with APP-processing

Arg	Glu	Lys	Lys	Lys	Ile	Leu	Leu	Asn	Ile	Glu	His	Arg	Ile	Met
	2255					2260					2265			
Leu	Arg	Met	Ala	Pro	Asp	Tyr	Asp	His	Leu	Thr	Leu	Met	Gln	Lys
	2270					2275					2280			
Val	Glu	Val	Phe	Glu	His	Ala	Val	Asn	Asn	Thr	Ala	Gly	Asp	Asp
	2285					2290					2295			
Leu	Ala	Lys	Leu	Leu	Trp	Leu	Lys	Ser	Pro	Ser	Ser	Glu	Val	Trp
	2300					2305					2310			
Phe	Asp	Arg	Arg	Thr	Asn	Tyr	Thr	Arg	Ser	Leu	Ala	Val	Met	Ser
	2315					2320					2325			
Met	Val	Gly	Tyr	Ile	Leu	Gly	Leu	Gly	Asp	Arg	His	Pro	Ser	Asn
	2330					2335					2340			
Leu	Met	Leu	Asp	Arg	Leu	Ser	Gly	Lys	Ile	Leu	His	Ile	Asp	Phe
	2345					2350					2355			
Gly	Asp	Cys	Phe	Glu	Val	Ala	Met	Thr	Arg	Glu	Lys	Phe	Pro	Glu
	2360					2365					2370			
Lys	Ile	Pro	Phe	Arg	Leu	Thr	Arg	Met	Leu	Thr	Asn	Ala	Met	Glu
	2375					2380					2385			
Val	Thr	Gly	Leu	Asp	Gly	Asn	Tyr	Arg	Ile	Thr	Cys	His	Thr	Val
	2390					2395					2400			
Met	Glu	Val	Leu	Arg	Glu	His	Lys	Asp	Ser	Val	Met	Ala	Val	Leu
	2405					2410					2415			
Glu	Ala	Phe	Val	Tyr	Asp	Pro	Leu	Leu	Asn	Trp	Arg	Leu	Met	Asp
	2420					2425					2430			
Thr	Asn	Thr	Lys	Gly	Asn	Lys	Arg	Ser	Arg	Thr	Arg	Thr	Asp	Ser
	2435					2440					2445			
Tyr	Ser	Ala	Gly	Gln	Ser	Val	Glu	Ile	Leu	Asp	Gly	Val	Glu	Leu
	2450					2455					2460			
Gly	Glu	Pro	Ala	His	Lys	Lys	Thr	Gly	Thr	Thr	Val	Pro	Glu	Ser
	2465					2470					2475			
Ile	His	Ser	Phe	Ile	Gly	Asp	Gly	Leu	Val	Lys	Pro	Glu	Ala	Leu
	2480					2485					2490			
Asn	Lys	Lys	Ala	Ile	Gln	Ile	Ile	Asn	Arg	Val	Arg	Asp	Lys	Leu
	2495					2500					2505			

Protein Complexes associated with APP-processing

Thr Gly Arg Asp Phe Ser His Asp Asp Thr Leu Asp Val Pro Thr
 2510 2515 2520

Gln Val Glu Leu Leu Ile Lys Gln Ala Thr Ser His Glu Asn Leu
 2525 2530 2535

Cys Gln Cys Tyr Ile Gly Trp Cys Pro Phe Trp
 2540 2545

<210> 59

<211> 443

<212> PRT

<213> Homo sapiens

<400> 59

Arg Gln Ala Trp His Glu Val Ala Ala Pro Ser Trp Arg Gly Ala Arg
 1 5 10 15

Leu Val Gln Ser Ala Leu Arg Val Trp Gln Val Gly Pro His Val Ala
 20 25 30

Arg Glu Arg Val Ile Pro Phe Ser Ser Leu Leu Gly Phe Gln Arg Arg
 35 40 45

Cys Val Ser Cys Val Ala Gly Ser Ala Phe Ser Gly Pro Arg Leu Ala
 50 55 60

Ser Ala Ser Arg Ser Asn Gly Gln Gly Ser Ala Leu Asp His Phe Leu
 65 70 75 80

Gly Phe Ser Gln Pro Asp Ser Ser Val Thr Pro Cys Val Pro Ala Val
 85 90 95

Ser Met Asn Arg Asp Glu Gln Asp Val Leu Leu Val His His Pro Asp
 100 105 110

Met Pro Glu Asn Ser Arg Val Leu Arg Val Val Leu Leu Gly Ala Pro
 115 120 125

Asn Ala Gly Lys Ser Thr Leu Ser Asn Gln Leu Leu Gly Arg Lys Val
 130 135 140

Phe Pro Val Ser Arg Lys Val His Thr Thr Arg Cys Gln Ala Leu Gly
 145 150 155 160

Val Ile Thr Glu Lys Glu Thr Gln Val Ile Leu Leu Asp Thr Pro Gly
 165 170 175

Protein Complexes associated with APP-processing

Ile Ile Ser Pro Gly Lys Gln Lys Arg His His Leu Glu Leu Ser Leu
180 185 190

Leu Glu Asp Pro Trp Lys Ser Met Glu Ser Ala Asp Leu Val Val Val
195 200 205

Leu Val Asp Val Ser Asp Lys Trp Thr Arg Asn Gln Leu Ser Pro Gln
210 215 220

Leu Leu Arg Cys Leu Thr Lys Tyr Ser Gln Ile Pro Ser Val Leu Val
225 230 235 240

Met Asn Lys Val Asp Cys Leu Lys Gln Lys Ser Val Leu Leu Glu Leu
245 250 255

Thr Ala Ala Leu Thr Glu Gly Val Val Asn Gly Lys Lys Leu Lys Met
260 265 270

Arg Gln Ala Phe His Ser His Pro Gly Thr His Cys Pro Ser Pro Ala
275 280 285

Val Lys Asp Pro Asn Thr Gln Ser Val Gly Asn Pro Gln Arg Ile Gly
290 295 300

Trp Pro His Phe Lys Glu Ile Phe Met Leu Ser Ala Leu Ser Gln Glu
305 310 315 320

Asp Val Lys Thr Leu Lys Gln Tyr Leu Leu Thr Gln Ala Gln Pro Gly
325 330 335

Pro Trp Glu Tyr His Ser Ala Val Leu Thr Ser Gln Thr Pro Glu Glu
340 345 350

Ile Cys Ala Asn Ile Ile Arg Glu Lys Leu Leu Glu His Leu Pro Gln
355 360 365

Glu Val Pro Tyr Asn Val Gln Gln Lys Thr Ala Val Trp Glu Glu Gly
370 375 380

Pro Gly Gly Glu Leu Val Ile Gln Gln Lys Leu Leu Val Pro Lys Glu
385 390 395 400

Ser Tyr Val Lys Leu Leu Ile Gly Pro Lys Gly His Val Ile Ser Gln
405 410 415

Ile Ala Gln Glu Ala Gly His Asp Leu Met Asp Ile Phe Leu Cys Asp
420 425 430

Val Asp Ile Arg Leu Ser Val Lys Leu Leu Lys
435 440

Protein Complexes associated with APP-processing

<210> 60

<211> 488

<212> PRT

<213> Homo sapiens

<400> 60

Met Ala Tyr Ser Gln Gly Gly Gly Lys Lys Lys Val Cys Tyr Tyr Tyr
 1 5 10 15

Asp Gly Asp Ile Gly Asn Tyr Tyr Tyr Gly Gln Gly His Pro Met Lys
 20 25 30

Pro His Arg Ile Arg Met Thr His Asn Leu Leu Leu Asn Tyr Gly Leu
 35 40 45

Tyr Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala Thr Ala Glu Glu
 50 55 60

Met Thr Lys Tyr His Ser Asp Glu Tyr Ile Lys Phe Leu Arg Ser Ile
 65 70 75 80

Arg Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met His Ile Phe Asn
 85 90 95

Val Gly Glu Asp Cys Pro Ala Phe Asp Gly Leu Phe Glu Phe Cys Gln
 100 105 110

Leu Ser Thr Gly Gly Ser Val Ala Gly Ala Val Lys Leu Asn Arg Gln
 115 120 125

Gln Thr Asp Met Ala Val Asn Trp Ala Gly Gly Leu His His Ala Lys
 130 135 140

Lys Tyr Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala
 145 150 155 160

Ile Leu Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr Ile Asp Ile
 165 170 175

Asp Ile His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp
 180 185 190

Arg Val Met Thr Val Ser Phe His Lys Tyr Gly Glu Tyr Phe Pro Gly
 195 200 205

Thr Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala
 210 215 220

Protein Complexes associated with APP-processing

Val Asn Phe Pro Met Cys Asp Gly Ile Asp Asp Glu Ser Tyr Gly Gln
 225 230 235 240

Ile Phe Lys Pro Ile Ile Ser Lys Val Met Glu Met Tyr Gln Pro Ser
 245 250 255

Ala Val Val Leu Gln Cys Gly Ala Asp Ser Leu Ser Gly Asp Arg Leu
 260 265 270

Gly Cys Phe Asn Leu Thr Val Lys Gly His Ala Lys Cys Val Glu Val
 275 280 285

Val Lys Thr Phe Asn Leu Pro Leu Leu Met Leu Gly Gly Gly Tyr
 290 295 300

Thr Ile Arg Asn Val Ala Arg Cys Trp Thr Tyr Glu Thr Ala Val Ala
 305 310 315 320

Leu Asp Cys Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu
 325 330 335

Tyr Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser Asn Met Thr
 340 345 350

Asn Gln Asn Thr Pro Glu Tyr Met Glu Lys Ile Lys Gln Arg Leu Phe
 355 360 365

Glu Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala
 370 375 380

Ile Pro Glu Asp Ala Val His Glu Asp Ser Gly Asp Glu Asp Gly Glu
 385 390 395 400

Asp Pro Asp Lys Arg Ile Ser Ile Arg Ala Ser Asp Lys Arg Ile Ala
 405 410 415

Cys Asp Glu Glu Phe Ser Asp Ser Glu Asp Glu Gly Glu Gly Gly Arg
 420 425 430

Arg Asn Val Ala Asp His Lys Lys Gly Ala Lys Lys Ala Arg Ile Glu
 435 440 445

Glu Asp Lys Lys Glu Thr Glu Asp Lys Lys Thr Asp Val Lys Glu Glu
 450 455 460

Asp Lys Ser Lys Asp Asn Ser Gly Glu Lys Thr Asp Thr Lys Gly Thr
 465 470 475 480

Lys Ser Glu Gln Leu Ser Asn Pro
 485

Protein Complexes associated with APP-processing

<210> 61

<211> 4834

<212> PRT

<213> Homo sapiens

<400> 61

Met Pro Ser Glu Ser Phe Cys Leu Ala Ala Gln Ala Arg Leu Asp Ser
 1 5 10 15

Lys Trp Leu Lys Thr Asp Ile Gln Leu Ala Phe Thr Arg Asp Gly Leu
 20 25 30

Cys Gly Leu Trp Asn Glu Met Val Lys Asp Gly Glu Ile Val Tyr Thr
 35 40 45

Gly Thr Glu Ser Thr Gln Asn Gly Glu Leu Pro Pro Arg Lys Asp Asp
 50 55 60

Ser Val Glu Pro Ser Gly Thr Lys Lys Glu Asp Leu Asn Asp Lys Glu
 65 70 75 80

Lys Lys Asp Glu Glu Glu Thr Pro Ala Pro Ile Tyr Arg Ala Lys Ser
 85 90 95

Ile Leu Asp Ser Trp Val Trp Gly Lys Gln Pro Asp Val Asn Glu Leu
 100 105 110

Lys Glu Cys Leu Ser Val Leu Val Lys Glu Gln Gln Ala Leu Ala Val
 115 120 125

Gln Ser Ala Thr Thr Thr Leu Ser Ala Leu Arg Leu Lys Gln Arg Leu
 130 135 140

Val Ile Leu Glu Arg Tyr Phe Ile Ala Leu Asn Arg Thr Val Phe Gln
 145 150 155 160

Glu Asn Val Lys Val Lys Trp Lys Ser Ser Gly Ile Ser Leu Pro Pro
 165 170 175

Val Asp Lys Lys Ser Ser Arg Pro Ala Gly Lys Gly Val Glu Gly Leu
 180 185 190

Ala Arg Val Gly Ser Arg Ala Ala Leu Ser Phe Ala Phe Ala Phe Leu
 195 200 205

Arg Arg Ala Trp Arg Ser Gly Glu Asp Ala Asp Leu Cys Ser Glu Leu
 210 215 220

Protein Complexes associated with APP-processing

Leu Gln Glu Ser Leu Asp Ala Leu Arg Ala Leu Pro Glu Ala Ser Leu
 225 230 235 240

Phe Asp Glu Ser Thr Val Ser Ser Val Trp Leu Glu Val Val Glu Arg
 245 250 255

Ala Thr Arg Phe Leu Arg Ser Val Val Thr Gly Asp Val His Gly Thr
 260 265 270

Pro Ala Thr Lys Gly Pro Gly Ser Ile Pro Leu Gln Asp Gln His Leu
 275 280 285

Ala Leu Ala Ile Leu Leu Glu Leu Ala Val Gln Arg Gly Thr Leu Ser
 290 295 300

Gln Met Leu Ser Ala Ile Leu Leu Leu Leu Gln Leu Trp Asp Ser Gly
 305 310 315 320

Ala Gln Glu Thr Asp Asn Glu Arg Ser Ala Gln Gly Thr Ser Ala Pro
 325 330 335

Leu Leu Pro Leu Leu Gln Arg Phe Gln Ser Ile Ile Cys Arg Lys Asp
 340 345 350

Ala Pro His Ser Glu Gly Asp Met His Leu Leu Ser Gly Pro Leu Ser
 355 360 365

Pro Asn Glu Ser Phe Leu Arg Tyr Leu Thr Leu Pro Gln Asp Asn Glu
 370 375 380

Leu Ala Ile Asp Leu Arg Gln Thr Ala Val Val Val Met Ala His Leu
 385 390 395 400

Asp Arg Leu Ala Thr Pro Cys Met Pro Pro Leu Cys Ser Ser Pro Thr
 405 410 415

Ser His Lys Gly Ser Leu Gln Glu Val Ile Gly Trp Gly Leu Ile Gly
 420 425 430

Trp Lys Tyr Tyr Ala Asn Val Ile Gly Pro Ile Gln Cys Glu Gly Leu
 435 440 445

Ala Asn Leu Gly Val Thr Gln Ile Ala Cys Ala Glu Lys Arg Phe Leu
 450 455 460

Ile Leu Ser Arg Asn Gly Arg Val Tyr Thr Gln Ala Tyr Asn Ser Asp
 465 470 475 480

Thr Leu Ala Pro Gln Leu Val Gln Gly Leu Ala Ser Arg Asn Ile Val
 485 490 495

Protein Complexes associated with APP-processing

Ala Ala Leu Pro Gly Leu Asp Thr Lys His Ile val Gly Ile Ala Cys
755 760 765

Protein Complexes associated with APP-processing
 Gly Pro Ala Gln Ser Phe Ala Trp Ser Ser Cys Ser Glu Trp Ser Ile
 770 775 780

Gly Leu Arg Val Pro Phe Val Val Asp Ile Cys Ser Met Thr Phe Glu
 785 790 795 800

Gln Leu Asp Leu Leu Leu Arg Gln Val Ser Glu Gly Met Asp Gly Ser
 805 810 815

Ala Asp Trp Pro Pro Pro Gln Glu Lys Glu Cys Val Ala Val Ala Thr
 820 825 830

Leu Asn Leu Leu Arg Leu Gln Leu His Ala Ala Ile Ser His Gln Val
 835 840 845

Asp Pro Glu Phe Leu Gly Leu Gly Leu Gly Ser Ile Leu Leu Asn Ser
 850 855 860

Leu Lys Gln Thr Val Val Thr Leu Ala Ser Ser Ala Gly Val Leu Ser
 865 870 875 880

Thr Val Gln Ser Ala Ala Gln Ala Val Leu Gln Ser Gly Trp Ser Val
 885 890 895

Leu Leu Pro Thr Ala Glu Glu Arg Ala Arg Ala Leu Ser Ala Leu Leu
 900 905 910

Pro Cys Ala Val Ser Gly Asn Glu Val Asn Ile Ser Pro Gly Arg Arg
 915 920 925

Phe Met Ile Asp Leu Leu Val Gly Ser Leu Met Ala Asp Gly Gly Leu
 930 935 940

Glu Ser Ala Leu His Ala Ala Ile Thr Ala Glu Ile Gln Asp Ile Glu
 945 950 955 960

Ala Lys Lys Glu Ala Gln Lys Glu Lys Glu Ile Asp Glu Gln Glu Ala
 965 970 975

Asn Ala Ser Thr Phe His Arg Ser Arg Thr Pro Leu Asp Lys Asp Leu
 980 985 990

Ile Asn Thr Gly Ile Cys Glu Ser Ser Gly Lys Gln Cys Leu Pro Leu
 995 1000 1005

Val Gln Leu Ile Gln Gln Leu Leu Arg Asn Ile Ala Ser Gln Thr
 1010 1015 1020

Val Ala Arg Leu Lys Asp Val Ala Arg Arg Ile Ser Ser Cys Leu
 1025 1030 1035

Protein Complexes associated with APP-processing

Asp Phe Glu Gln His Ser Arg Glu Arg Ser Ala Ser Leu Asp Trp
 1040 1045 1050

Leu Leu Arg Phe Gln Arg Leu Leu Ile Ser Lys Leu Tyr Pro Gly
 1055 1060 1065

Glu Ser Ile Gly Gln Thr Ser Asp Ile Ser Ser Pro Glu Leu Met
 1070 1075 1080

Gly Val Gly Ser Leu Leu Lys Lys Tyr Thr Ala Leu Leu Cys Thr
 1085 1090 1095

His Ile Gly Asp Ile Leu Pro Val Ala Ala Ser Ile Ala Ser Thr
 1100 1105 1110

Ser Trp Arg His Phe Ala Glu Val Ala Tyr Ile Val Glu Gly Asp
 1115 1120 1125

Phe Thr Gly Val Leu Leu Pro Glu Leu Val Val Ser Ile Val Leu
 1130 1135 1140

Leu Leu Ser Lys Asn Ala Asp Leu Met Gln Glu Ala Gly Ala Val
 1145 1150 1155

Pro Leu Leu Gly Gly Leu Leu Glu His Leu Asp Arg Phe Asn His
 1160 1165 1170

Leu Ala Pro Gly Lys Glu Arg Asp Asp His Glu Glu Leu Ala Trp
 1175 1180 1185

Pro Gly Ile Met Glu Ser Phe Phe Thr Gly Gln Asn Cys Arg Asn
 1190 1195 1200

Asn Glu Glu Val Thr Leu Ile Arg Lys Ala Asp Leu Glu Asn His
 1205 1210 1215

Asn Lys Asp Gly Gly Phe Trp Thr Val Ile Asp Gly Lys Val Tyr
 1220 1225 1230

Asp Ile Lys Asp Phe Gln Thr Gln Ser Leu Thr Gly Asn Ser Ile
 1235 1240 1245

Leu Ala Gln Phe Ala Gly Glu Asp Pro Val Val Ala Leu Glu Ala
 1250 1255 1260

Ala Leu Gln Phe Glu Asp Thr Arg Glu Ser Met His Ala Phe Cys
 1265 1270 1275

Val Gly Gln Tyr Leu Glu Pro Asp Gln Glu Ile Val Thr Ile Pro
 1280 1285 1290

Protein Complexes associated with APP-processing

Asp Leu Gly Ser Leu Ser Ser Pro Leu Ile Asp Thr Glu Arg Asn
 1295 1300 1305

Leu Gly Leu Leu Leu Gly Leu His Ala Ser Tyr Leu Ala Met Ser
 1310 1315 1320

Thr Pro Leu Ser Pro Val Glu Ile Glu Cys Ala Lys Trp Leu Gln
 1325 1330 1335

Ser Ser Ile Phe Ser Gly Gly Leu Gln Thr Ser Gln Ile His Tyr
 1340 1345 1350

Arg Tyr Asn Glu Glu Lys Asp Glu Asp His Cys Ser Ser Pro Gly
 1355 1360 1365

Gly Thr Pro Ala Ser Lys Ser Arg Leu Cys Ser His Arg Arg Ala
 1370 1375 1380

Leu Gly Asp His Ser Gln Ala Phe Leu Gln Ala Ile Ala Asp Asn
 1385 1390 1395

Asn Ile Gln Asp His Asn Val Lys Asp Phe Leu Cys Gln Ile Glu
 1400 1405 1410

Arg Tyr Cys Arg Gln Cys His Leu Thr Thr Pro Ile Met Phe Pro
 1415 1420 1425

Pro Glu His Pro Val Glu Glu Val Gly Arg Leu Leu Leu Cys Cys
 1430 1435 1440

Leu Leu Lys His Glu Asp Leu Gly His Val Ala Leu Ser Leu Val
 1445 1450 1455

His Ala Gly Ala Leu Gly Ile Glu Gln Val Lys His Arg Thr Leu
 1460 1465 1470

Pro Lys Ser Val Val Asp Val Cys Arg Val Val Tyr Gln Ala Lys
 1475 1480 1485

Cys Ser Leu Ile Lys Thr His Gln Glu Gln Gly Arg Ser Tyr Lys
 1490 1495 1500

Glu Val Cys Ala Pro Val Ile Glu Arg Leu Arg Phe Leu Phe Asn
 1505 1510 1515

Glu Leu Arg Pro Ala Val Cys Asn Asp Leu Ser Ile Met Ser Lys
 1520 1525 1530

Phe Lys Leu Leu Ser Ser Leu Pro Arg Trp Arg Arg Ile Ala Gln
 1535 1540 1545

Protein Complexes associated with APP-processing

Lys Ile Ile Arg Glu Arg Arg Lys Lys Arg Val Pro Lys Lys Pro
 1550 1555 1560

Glu Ser Met Asp Asp Glu Glu Lys Ile Gly Asn Glu Glu Ser Asp
 1565 1570 1575

Leu Glu Glu Ala Cys Ile Leu Pro His Ser Pro Ile Asn Val Asp
 1580 1585 1590

Lys Arg Pro Ile Ala Ile Lys Ser Pro Lys Asp Lys Trp Gln Pro
 1595 1600 1605

Leu Leu Ser Thr Val Thr Gly Val His Lys Tyr Lys Trp Leu Lys
 1610 1615 1620

Gln Asn Val Gln Gly Leu Tyr Pro Gln Ser Pro Leu Leu Ser Thr
 1625 1630 1635

Ile Ala Glu Phe Ala Leu Lys Glu Glu Pro Val Asp Val Glu Lys
 1640 1645 1650

Met Arg Lys Cys Leu Leu Lys Gln Leu Glu Arg Ala Glu Val Arg
 1655 1660 1665

Leu Glu Gly Ile Asp Thr Ile Leu Lys Leu Ala Ser Lys Asn Phe
 1670 1675 1680

Leu Leu Pro Ser Val Gln Tyr Ala Met Phe Cys Gly Trp Gln Arg
 1685 1690 1695

Leu Ile Pro Glu Gly Ile Asp Ile Gly Glu Pro Leu Thr Asp Cys
 1700 1705 1710

Leu Lys Asp Val Asp Leu Ile Pro Pro Phe Asn Arg Met Leu Leu
 1715 1720 1725

Glu Val Thr Phe Gly Lys Leu Tyr Ala Trp Ala Val Gln Asn Ile
 1730 1735 1740

Arg Asn Val Leu Met Asp Ala Ser Ala Thr Phe Lys Glu Leu Gly
 1745 1750 1755

Ile Gln Pro Val Pro Leu Gln Thr Ile Thr Asn Glu Asn Pro Ser
 1760 1765 1770

Gly Pro Ser Leu Gly Thr Ile Pro Gln Ala Arg Phe Leu Leu Val
 1775 1780 1785

Met Leu Ser Met Leu Thr Leu Gln His Gly Ala Asn Asn Leu Asp
 1790 1795 1800

Protein Complexes associated with APP-processing

Leu	Leu	Leu	Asn	Ser	Gly	Met	Leu	Ala	Leu	Thr	Gln	Thr	Ala	Leu
	1805					1810					1815			
Arg	Leu	Ile	Gly	Pro	Ser	Cys	Asp	Asn	Val	Glu	Glu	Asp	Met	Asn
	1820					1825					1830			
Ala	Ser	Ala	Gln	Gly	Ala	Ser	Ala	Thr	Val	Leu	Glu	Glu	Thr	Arg
	1835					1840					1845			
Lys	Glu	Thr	Ala	Pro	Val	Gln	Leu	Pro	Val	Ser	Gly	Pro	Glu	Leu
	1850					1855					1860			
Ala	Ala	Met	Met	Lys	Ile	Gly	Thr	Arg	Val	Met	Arg	Gly	Val	Asp
	1865					1870					1875			
Trp	Lys	Trp	Gly	Asp	Gln	Asp	Gly	Pro	Pro	Pro	Gly	Leu	Gly	Arg
	1880					1885					1890			
Val	Ile	Gly	Glu	Leu	Gly	Glu	Asp	Gly	Trp	Ile	Arg	Val	Gln	Trp
	1895					1900					1905			
Asp	Thr	Gly	Ser	Thr	Asn	Ser	Tyr	Arg	Met	Gly	Lys	Glu	Gly	Lys
	1910					1915					1920			
Tyr	Asp	Leu	Lys	Leu	Ala	Glu	Leu	Pro	Ala	Ala	Ala	Gln	Pro	Ser
	1925					1930					1935			
Ala	Glu	Asp	Ser	Asp	Thr	Glu	Asp	Asp	Ser	Glu	Ala	Glu	Gln	Thr
	1940					1945					1950			
Glu	Arg	Asn	Ile	His	Pro	Thr	Ala	Met	Met	Phe	Thr	Ser	Thr	Ile
	1955					1960					1965			
Asn	Leu	Leu	Gln	Thr	Leu	Cys	Leu	Ser	Ala	Gly	Val	His	Ala	Glu
	1970					1975					1980			
Ile	Met	Gln	Ser	Glu	Ala	Thr	Lys	Thr	Leu	Cys	Gly	Leu	Leu	Arg
	1985					1990					1995			
Met	Leu	Val	Glu	Ser	Gly	Thr	Thr	Asp	Lys	Thr	Ser	Ser	Pro	Asn
	2000					2005					2010			
Arg	Leu	Val	Tyr	Arg	Glu	Gln	His	Arg	Ser	Trp	Cys	Thr	Leu	Gly
	2015					2020					2025			
Phe	Val	Arg	Ser	Ile	Ala	Leu	Thr	Pro	Gln	Val	Cys	Gly	Ala	Leu
	2030					2035					2040			
Ser	Ser	Pro	Gln	Trp	Ile	Thr	Leu	Leu	Met	Lys	Val	Val	Glu	Gly
	2045					2050					2055			

Protein Complexes associated with APP-processing
 His Ala Pro Phe Thr Ala Thr Ser Leu Gln Arg Gln Ile Leu Ala
 2060 2065 2070

Val His Leu Leu Gln Ala Val Leu Pro Ser Trp Asp Lys Thr Glu
 2075 2080 2085

Arg Ala Arg Asp Met Lys Cys Leu Val Glu Lys Leu Phe Asp Phe
 2090 2095 2100

Leu Gly Ser Leu Leu Thr Thr Cys Ser Ser Asp Val Pro Leu Leu
 2105 2110 2115

Arg Glu Ser Thr Leu Arg Arg Arg Arg Val Arg Pro Gln Ala Ser
 2120 2125 2130

Leu Thr Ala Thr His Ser Ser Thr Leu Ala Glu Glu Val Val Ala
 2135 2140 2145

Leu Leu Arg Thr Leu His Ser Leu Thr Gln Trp Asn Gly Leu Ile
 2150 2155 2160

Asn Lys Tyr Ile Asn Ser Gln Leu Arg Ser Ile Thr His Ser Phe
 2165 2170 2175

Val Gly Arg Pro Ser Glu Gly Ala Gln Leu Glu Asp Tyr Phe Pro
 2180 2185 2190

Asp Ser Glu Asn Pro Glu Val Gly Gly Leu Met Ala Val Leu Ala
 2195 2200 2205

Val Ile Gly Gly Ile Asp Gly Arg Leu Arg Leu Gly Gly Gln Val
 2210 2215 2220

Met His Asp Glu Phe Gly Glu Gly Thr Val Thr Arg Ile Thr Pro
 2225 2230 2235

Lys Gly Lys Ile Thr Val Gln Phe Ser Asp Met Arg Thr Cys Arg
 2240 2245 2250

Val Cys Pro Leu Asn Gln Leu Lys Pro Leu Pro Ala Val Ala Phe
 2255 2260 2265

Asn Val Asn Asn Leu Pro Phe Thr Glu Pro Met Leu Ser Val Trp
 2270 2275 2280

Ala Gln Leu Val Asn Leu Ala Gly Ser Lys Leu Glu Lys His Lys
 2285 2290 2295

Ile Lys Lys Ser Thr Lys Gln Ala Phe Ala Gly Gln Val Asp Leu
 2300 2305 2310

Protein Complexes associated with APP-processing

Asp Leu Leu Arg Cys Gln Gln Leu Lys Leu Tyr Ile Leu Lys Ala
 2315 2320 2325

Gly Arg Ala Leu Leu Ser His Gln Asp Lys Leu Arg Gln Ile Leu
 2330 2335 2340

Ser Gln Pro Ala Val Gln Glu Thr Gly Thr Val His Thr Asp Asp
 2345 2350 2355

Gly Ala Val Val Ser Pro Asp Leu Gly Asp Met Ser Pro Glu Gly
 2360 2365 2370

Pro Gln Pro Pro Met Ile Leu Leu Gln Gln Leu Leu Ala Ser Ala
 2375 2380 2385

Thr Gln Pro Ser Pro Val Lys Ala Ile Phe Asp Lys Gln Glu Leu
 2390 2395 2400

Glu Ala Ala Ala Leu Ala Val Cys Gln Cys Leu Ala Val Glu Ser
 2405 2410 2415

Thr His Pro Ser Ser Pro Gly Phe Glu Asp Cys Ser Ser Ser Glu
 2420 2425 2430

Ala Thr Thr Pro Val Ala Val Gln His Ile His Pro Ala Arg Val
 2435 2440 2445

Lys Arg Arg Lys Gln Ser Pro Val Pro Ala Leu Pro Ile Val Val
 2450 2455 2460

Gln Leu Met Glu Met Gly Phe Ser Arg Arg Asn Ile Glu Phe Ala
 2465 2470 2475

Leu Lys Ser Leu Thr Gly Ala Ser Gly Asn Ala Ser Ser Leu Pro
 2480 2485 2490

Gly Val Glu Ala Leu Val Gly Trp Leu Leu Asp His Ser Asp Ile
 2495 2500 2505

Gln Val Thr Glu Leu Ser Asp Ala Asp Thr Val Ser Asp Glu Tyr
 2510 2515 2520

Ser Asp Glu Glu Val Val Glu Asp Val Asp Asp Ala Ala Tyr Ser
 2525 2530 2535

Met Ser Thr Gly Ala Val Val Thr Glu Ser Gln Thr Tyr Lys Lys
 2540 2545 2550

Arg Ala Asp Phe Leu Ser Asn Asp Asp Tyr Ala Val Tyr Val Arg
 2555 2560 2565

Protein Complexes associated with APP-processing
 Glu Asn Ile Gln Val Gly Met Met Val Arg Cys Cys Arg Ala Tyr
 2570 2575 2580

Glu Glu Val Cys Glu Gly Asp Val Gly Lys Val Ile Lys Leu Asp
 2585 2590 2595

Arg Asp Gly Leu His Asp Leu Asn Val Gln Cys Asp Trp Gln Gln
 2600 2605 2610

Lys Gly Gly Thr Tyr Trp Val Arg Tyr Ile His Val Glu Leu Ile
 2615 2620 2625

Gly Tyr Pro Pro Pro Ser Ser Ser Ser His Ile Lys Ile Gly Asp
 2630 2635 2640

Lys Val Arg Val Lys Ala Ser Val Thr Thr Pro Lys Tyr Lys Trp
 2645 2650 2655

Gly Ser Val Thr His Gln Ser Val Gly Val Val Lys Ala Phe Ser
 2660 2665 2670

Ala Asn Gly Lys Asp Ile Ile Val Asp Phe Pro Gln Gln Ser His
 2675 2680 2685

Trp Thr Gly Leu Leu Ser Glu Met Glu Leu Val Pro Ser Ile His
 2690 2695 2700

Pro Gly Val Thr Cys Asp Gly Cys Gln Met Phe Pro Ile Asn Gly
 2705 2710 2715

Ser Arg Phe Lys Cys Arg Asn Cys Asp Asp Phe Asp Phe Cys Glu
 2720 2725 2730

Thr Cys Phe Lys Thr Lys Lys His Asn Thr Arg His Thr Phe Gly
 2735 2740 2745

Arg Ile Asn Glu Pro Gly Gln Ser Ala Val Phe Cys Gly Arg Ser
 2750 2755 2760

Gly Lys Gln Leu Lys Arg Cys His Ser Ser Gln Pro Gly Met Leu
 2765 2770 2775

Leu Asp Ser Trp Ser Arg Met Val Lys Ser Leu Asn Val Ser Ser
 2780 2785 2790

Ser Val Asn Gln Ala Ser Arg Leu Ile Asp Gly Ser Glu Pro Cys
 2795 2800 2805

Trp Gln Ser Ser Gly Ser Gln Gly Lys His Trp Ile Arg Leu Glu
 2810 2815 2820

Protein Complexes associated with APP-processing

Ile	Phe	Pro	Asp	Val	Leu	Val	His	Arg	Leu	Lys	Met	Ile	Val	Asp
	2825					2830					2835			
Pro	Ala	Asp	Ser	Ser	Tyr	Met	Pro	Ser	Leu	Val	Val	Val	Ser	Gly
	2840					2845					2850			
Gly	Asn	Ser	Leu	Asn	Asn	Leu	Ile	Glu	Leu	Lys	Thr	Ile	Asn	Ile
	2855					2860					2865			
Asn	Pro	Ser	Asp	Thr	Thr	Val	Pro	Leu	Leu	Asn	Asp	Tyr	Thr	Glu
	2870					2875					2880			
Tyr	His	Arg	Tyr	Ile	Glu	Ile	Ala	Ile	Lys	Gln	Cys	Arg	Ser	Ser
	2885					2890					2895			
Gly	Ile	Asp	Cys	Lys	Ile	His	Gly	Leu	Ile	Leu	Leu	Gly	Arg	Ile
	2900					2905					2910			
Arg	Ala	Glu	Glu	Glu	Asp	Leu	Ala	Ala	Val	Pro	Phe	Leu	Ala	Ser
	2915					2920					2925			
Asp	Asn	Glu	Glu	Glu	Glu	Asp	Glu	Lys	Gly	Asn	Ser	Gly	Ser	Leu
	2930					2935					2940			
Ile	Arg	Lys	Lys	Ala	Ala	Gly	Leu	Glu	Ser	Ala	Ala	Thr	Ile	Arg
	2945					2950					2955			
Thr	Lys	Val	Phe	Val	Trp	Gly	Leu	Asn	Asp	Lys	Asp	Gln	Leu	Gly
	2960					2965					2970			
Gly	Leu	Lys	Gly	Ser	Lys	Ile	Lys	Val	Pro	Ser	Phe	Ser	Glu	Thr
	2975					2980					2985			
Leu	Ser	Ala	Leu	Asn	Val	Val	Gln	Val	Ala	Gly	Gly	Ser	Lys	Ser
	2990					2995					3000			
Leu	Phe	Ala	Val	Thr	Val	Glu	Gly	Lys	Val	Tyr	Ala	Cys	Gly	Glu
	3005					3010					3015			
Ala	Thr	Asn	Gly	Arg	Leu	Gly	Leu	Gly	Ile	Ser	Ser	Gly	Thr	Val
	3020					3025					3030			
Pro	Ile	Pro	Arg	Gln	Ile	Thr	Ala	Leu	Ser	Ser	Tyr	Val	Val	Lys
	3035					3040					3045			
Lys	Val	Ala	Val	His	Ser	Gly	Gly	Arg	His	Ala	Thr	Ala	Leu	Thr
	3050					3055					3060			
Val	Asp	Gly	Lys	Val	Phe	Ser	Trp	Gly	Glu	Gly	Asp	Asp	Gly	Lys
	3065					3070					3075			

Protein Complexes associated with APP-processing

Leu Gly His Phe Ser Arg Met Asn Cys Asp Lys Pro Arg Leu Ile
 3080 3085 3090

Glu Ala Leu Lys Thr Lys Arg Ile Arg Asp Ile Ala Cys Gly Ser
 3095 3100 3105

Ser His Ser Ala Ala Leu Thr Ser Ser Gly Glu Leu Tyr Thr Trp
 3110 3115 3120

Gly Leu Gly Glu Tyr Gly Arg Leu Gly His Gly Asp Asn Thr Thr
 3125 3130 3135

Gln Leu Lys Pro Lys Met Val Lys Val Leu Leu Gly His Arg Val
 3140 3145 3150

Ile Gln Val Ala Cys Gly Ser Arg Asp Ala Gln Thr Leu Ala Leu
 3155 3160 3165

Thr Asp Glu Gly Leu Val Phe Ser Trp Gly Asp Gly Asp Phe Gly
 3170 3175 3180

Lys Leu Gly Arg Gly Gly Ser Glu Gly Cys Asn Ile Pro Gln Asn
 3185 3190 3195

Ile Glu Arg Leu Asn Gly Gln Gly Val Cys Gln Ile Glu Cys Gly
 3200 3205 3210

Ala Gln Phe Ser Leu Ala Leu Thr Lys Ser Gly Val Val Trp Thr
 3215 3220 3225

Trp Gly Lys Gly Asp Tyr Phe Arg Leu Gly His Gly Ser Asp Val
 3230 3235 3240

His Val Arg Lys Pro Gln Val Val Glu Gly Leu Arg Gly Lys Lys
 3245 3250 3255

Ile Val His Val Ala Val Gly Ala Leu His Cys Leu Ala Val Thr
 3260 3265 3270

Asp Ser Gly Gln Val Tyr Ala Trp Gly Asp Asn Asp His Gly Gln
 3275 3280 3285

Gln Gly Asn Gly Thr Thr Thr Val Asn Arg Lys Pro Thr Leu Val
 3290 3295 3300

Gln Gly Leu Glu Gly Gln Lys Ile Thr Arg Val Ala Cys Gly Ser
 3305 3310 3315

Ser His Ser Val Ala Trp Thr Thr Val Asp Val Ala Thr Pro Ser
 3320 3325 3330

Protein Complexes associated with APP-processing

Val	His	Glu	Pro	Val	Leu	Phe	Gln	Thr	Ala	Arg	Asp	Pro	Leu	Gly
	3335					3340					3345			
Ala	Ser	Tyr	Leu	Gly	Val	Pro	Ser	Asp	Ala	Asp	Ser	Ser	Ala	Ala
	3350					3355					3360			
Ser	Asn	Lys	Ile	Ser	Gly	Ala	Ser	Asn	Ser	Lys	Pro	Asn	Arg	Pro
	3365					3370					3375			
Ser	Leu	Ala	Lys	Ile	Leu	Leu	Ser	Leu	Asp	Gly	Asn	Leu	Ala	Lys
	3380					3385					3390			
Gln	Gln	Ala	Leu	Ser	His	Ile	Leu	Thr	Ala	Leu	Gln	Ile	Met	Tyr
	3395					3400					3405			
Ala	Arg	Asp	Ala	Val	Val	Gly	Ala	Leu	Met	Pro	Ala	Ala	Met	Ile
	3410					3415					3420			
Ala	Pro	Val	Glu	Cys	Pro	Ser	Phe	Ser	Ser	Ala	Ala	Pro	Ser	Asp
	3425					3430					3435			
Ala	Ser	Ala	Met	Ala	Ser	Pro	Met	Asn	Gly	Glu	Glu	Cys	Met	Leu
	3440					3445					3450			
Ala	Val	Asp	Ile	Glu	Asp	Arg	Leu	Ser	Pro	Asn	Pro	Trp	Gln	Glu
	3455					3460					3465			
Lys	Arg	Glu	Ile	Val	Ser	Ser	Glu	Asp	Ala	Val	Thr	Pro	Ser	Ala
	3470					3475					3480			
Val	Thr	Pro	Ser	Ala	Pro	Ser	Ala	Ser	Ala	Arg	Pro	Phe	Ile	Pro
	3485					3490					3495			
Val	Thr	Asp	Asp	Leu	Gly	Ala	Ala	Ser	Ile	Ile	Ala	Glu	Thr	Met
	3500					3505					3510			
Thr	Lys	Thr	Lys	Glu	Asp	Val	Glu	Ser	Gln	Asn	Lys	Ala	Ala	Gly
	3515					3520					3525			
Pro	Glu	Pro	Gln	Ala	Leu	Asp	Glu	Phe	Thr	Ser	Leu	Leu	Ile	Ala
	3530					3535					3540			
Asp	Asp	Thr	Arg	Val	Val	Val	Asp	Leu	Leu	Lys	Leu	Ser	Val	Cys
	3545					3550					3555			
Ser	Arg	Ala	Gly	Asp	Arg	Gly	Arg	Asp	Val	Leu	Ser	Ala	Val	Leu
	3560					3565					3570			
Ser	Gly	Met	Gly	Thr	Ala	Tyr	Pro	Gln	Val	Ala	Asp	Met	Leu	Leu
	3575					3580					3585			

Protein Complexes associated with APP-processing

Glu	Leu	Cys	Val	Thr	Glu	Leu	Glu	Asp	Val	Ala	Thr	Asp	Ser	Gln
	3590					3595						3600		
Ser	Gly	Arg	Leu	Ser	Ser	Gln	Pro	Val	Val	Val	Glu	Ser	Ser	His
	3605					3610					3615			
Pro	Tyr	Thr	Asp	Asp	Thr	Ser	Thr	Ser	Gly	Thr	Val	Lys	Ile	Pro
	3620					3625					3630			
Gly	Ala	Glu	Gly	Leu	Arg	Val	Glu	Phe	Asp	Arg	Gln	Cys	Ser	Thr
	3635					3640					3645			
Glu	Arg	Arg	His	Asp	Pro	Leu	Thr	Val	Met	Asp	Gly	Val	Asn	Arg
	3650					3655					3660			
Ile	Val	Ser	Val	Arg	Ser	Gly	Arg	Glu	Trp	Ser	Asp	Trp	Ser	Ser
	3665					3670					3675			
Glu	Leu	Arg	Ile	Pro	Gly	Asp	Glu	Leu	Lys	Trp	Lys	Phe	Ile	Ser
	3680					3685					3690			
Asp	Gly	Ser	Val	Asn	Gly	Trp	Gly	Trp	Arg	Phe	Thr	Val	Tyr	Pro
	3695					3700					3705			
Ile	Met	Pro	Ala	Ala	Gly	Pro	Lys	Glu	Leu	Leu	Ser	Asp	Arg	Cys
	3710					3715					3720			
Val	Leu	Ser	Cys	Pro	Ser	Met	Asp	Leu	Val	Thr	Cys	Leu	Leu	Asp
	3725					3730					3735			
Phe	Arg	Leu	Asn	Leu	Ala	Ser	Asn	Arg	Ser	Ile	Val	Pro	Arg	Leu
	3740					3745					3750			
Ala	Ala	Ser	Leu	Ala	Ala	Cys	Ala	Gln	Leu	Ser	Ala	Leu	Ala	Ala
	3755					3760					3765			
Ser	His	Arg	Met	Trp	Ala	Leu	Gln	Arg	Leu	Arg	Lys	Leu	Leu	Thr
	3770					3775					3780			
Thr	Glu	Phe	Gly	Gln	Ser	Ile	Asn	Ile	Asn	Arg	Leu	Leu	Gly	Glu
	3785					3790					3795			
Asn	Asp	Gly	Glu	Thr	Arg	Ala	Leu	Ser	Phe	Thr	Gly	Ser	Ala	Leu
	3800					3805					3810			
Ala	Ala	Leu	Val	Lys	Gly	Leu	Pro	Glu	Ala	Leu	Gln	Arg	Gln	Phe
	3815					3820					3825			
Glu	Tyr	Glu	Asp	Pro	Ile	Val	Arg	Gly	Gly	Lys	Gln	Leu	Leu	His
	3830					3835					3840			

Protein Complexes associated with APP-processing

Ser	Pro	Phe	Phe	Lys	Val	Leu	Val	Ala	Leu	Ala	Cys	Asp	Leu	Glu
	3845					3850					3855			
Leu	Asp	Thr	Leu	Pro	Cys	Cys	Ala	Glu	Thr	His	Lys	Trp	Ala	Trp
	3860					3865					3870			
Phe	Arg	Arg	Tyr	Cys	Met	Ala	Ser	Arg	Val	Ala	Val	Ala	Leu	Asp
	3875					3880					3885			
Lys	Arg	Thr	Pro	Leu	Pro	Arg	Leu	Phe	Leu	Asp	Glu	Val	Ala	Lys
	3890					3895					3900			
Lys	Ile	Arg	Glu	Leu	Met	Ala	Asp	Ser	Glu	Asn	Met	Asp	Val	Leu
	3905					3910					3915			
His	Glu	Ser	His	Asp	Ile	Phe	Lys	Arg	Glu	Gln	Asp	Glu	Gln	Leu
	3920					3925					3930			
Val	Gln	Trp	Met	Asn	Arg	Arg	Pro	Asp	Asp	Trp	Thr	Leu	Ser	Ala
	3935					3940					3945			
Gly	Gly	Ser	Gly	Thr	Ile	Tyr	Gly	Trp	Gly	His	Asn	His	Arg	Gly
	3950					3955					3960			
Gln	Leu	Gly	Gly	Ile	Glu	Gly	Ala	Lys	Val	Lys	Val	Pro	Thr	Pro
	3965					3970					3975			
Cys	Glu	Ala	Leu	Ala	Thr	Leu	Arg	Pro	Val	Gln	Leu	Ile	Gly	Gly
	3980					3985					3990			
Glu	Gln	Thr	Leu	Phe	Ala	Val	Thr	Ala	Asp	Gly	Lys	Leu	Tyr	Ala
	3995					4000					4005			
Thr	Gly	Tyr	Gly	Ala	Gly	Gly	Arg	Leu	Gly	Ile	Gly	Gly	Thr	Glu
	4010					4015					4020			
Ser	Val	Ser	Thr	Pro	Thr	Leu	Leu	Glu	Ser	Ile	Gln	His	Val	Phe
	4025					4030					4035			
Ile	Lys	Lys	Val	Ala	Val	Asn	Ser	Gly	Gly	Lys	His	Cys	Leu	Ala
	4040					4045					4050			
Leu	Ser	Ser	Glu	Gly	Glu	Val	Tyr	Ser	Trp	Gly	Glu	Ala	Glu	Asp
	4055					4060					4065			
Gly	Lys	Leu	Gly	His	Gly	Asn	Arg	Ser	Pro	Cys	Asp	Arg	Pro	Arg
	4070					4075					4080			
Val	Ile	Glu	Ser	Leu	Arg	Gly	Ile	Glu	Val	Val	Asp	Val	Ala	Ala
	4085					4090					4095			

Protein Complexes associated with APP-processing

Gly Gly Ala His Ser Ala Cys Val Thr Ala Ala Gly Asp Leu Tyr
 4100 4105 4110

Thr Trp Gly Lys Gly Arg Tyr Gly Arg Leu Gly His Ser Asp Ser
 4115 4120 4125

Glu Asp Gln Leu Lys Pro Lys Leu Val Glu Ala Leu Gln Gly His
 4130 4135 4140

Arg Val Val Asp Ile Ala Cys Gly Ser Gly Asp Ala Gln Thr Leu
 4145 4150 4155

Cys Leu Thr Asp Asp Asp Thr Val Trp Ser Trp Gly Asp Gly Asp
 4160 4165 4170

Tyr Gly Lys Leu Gly Arg Gly Gly Ser Asp Gly Cys Lys Val Pro
 4175 4180 4185

Met Lys Ile Asp Ser Leu Thr Gly Leu Gly Val Val Lys Val Glu
 4190 4195 4200

Cys Gly Ser Gln Phe Ser Val Ala Leu Thr Lys Ser Gly Ala Val
 4205 4210 4215

Tyr Thr Trp Gly Lys Gly Asp Tyr His Arg Leu Gly His Gly Ser
 4220 4225 4230

Asp Asp His Val Arg Arg Pro Arg Gln Val Gln Gly Leu Gln Gly
 4235 4240 4245

Lys Lys Val Ile Ala Ile Ala Thr Gly Ser Leu His Cys Val Cys
 4250 4255 4260

Cys Thr Glu Asp Gly Glu Val Tyr Thr Trp Gly Asp Asn Asp Glu
 4265 4270 4275

Gly Gln Leu Gly Asp Gly Thr Thr Asn Ala Ile Gln Arg Pro Arg
 4280 4285 4290

Leu Val Ala Ala Leu Gln Gly Lys Lys Val Asn Arg Val Ala Cys
 4295 4300 4305

Gly Ser Ala His Thr Leu Ala Trp Ser Thr Ser Lys Pro Ala Ser
 4310 4315 4320

Ala Gly Lys Leu Pro Ala Gln Val Pro Met Glu Tyr Asn His Leu
 4325 4330 4335

Gln Glu Ile Pro Ile Ile Ala Leu Arg Asn Arg Leu Leu Leu Leu
 4340 4345 4350

Protein Complexes associated with APP-processing
 His His Leu Ser Glu Leu Phe Cys Pro Cys Ile Pro Met Phe Asp
 4355 4360 4365

Leu Glu Gly Ser Leu Asp Glu Thr Gly Leu Gly Pro Ser Val Gly
 4370 4375 4380

Phe Asp Thr Leu Arg Gly Ile Leu Ile Ser Gln Gly Lys Glu Ala
 4385 4390 4395

Ala Phe Arg Lys Val Val Gln Ala Thr Met Val Arg Asp Arg Gln
 4400 4405 4410

His Gly Pro Val Val Glu Leu Asn Arg Ile Gln Val Lys Arg Ser
 4415 4420 4425

Arg Ser Lys Gly Gly Leu Ala Gly Pro Asp Gly Thr Lys Ser Val
 4430 4435 4440

Phe Gly Gln Met Cys Ala Lys Met Ser Ser Phe Gly Pro Asp Ser
 4445 4450 4455

Leu Leu Leu Pro His Arg Val Trp Lys Val Lys Phe Val Gly Glu
 4460 4465 4470

Ser Val Asp Asp Cys Gly Gly Gly Tyr Ser Glu Ser Ile Ala Glu
 4475 4480 4485

Ile Cys Glu Glu Leu Gln Asn Gly Leu Thr Pro Leu Leu Ile Val
 4490 4495 4500

Thr Pro Asn Gly Arg Asp Glu Ser Gly Ala Asn Arg Asp Cys Tyr
 4505 4510 4515

Leu Leu Ser Pro Ala Ala Arg Ala Pro Val His Ser Ser Met Phe
 4520 4525 4530

Arg Phe Leu Gly Val Leu Leu Gly Ile Ala Ile Arg Thr Gly Ser
 4535 4540 4545

Pro Leu Ser Leu Asn Leu Ala Glu Pro Val Trp Lys Gln Leu Ala
 4550 4555 4560

Gly Met Ser Leu Thr Ile Ala Asp Leu Ser Glu Val Asp Lys Asp
 4565 4570 4575

Phe Ile Pro Gly Leu Met Tyr Ile Arg Asp Asn Glu Ala Thr Ser
 4580 4585 4590

Glu Glu Phe Glu Ala Met Ser Leu Pro Phe Thr Val Pro Ser Ala
 4595 4600 4605

Protein Complexes associated with APP-processing
 Ser Gly Gln Asp Ile Gln Leu Ser Ser Lys His Thr His Ile Thr
 4610 4615 4620

Leu Asp Asn Arg Ala Glu Tyr Val Arg Leu Ala Ile Asn Tyr Arg
 4625 4630 4635

Leu His Glu Phe Asp Glu Gln Val Ala Ala Val Arg Glu Gly Met
 4640 4645 4650

Ala Arg Val Val Pro Val Pro Leu Leu Ser Leu Phe Thr Gly Tyr
 4655 4660 4665

Glu Leu Glu Thr Met Val Cys Gly Ser Pro Asp Ile Pro Leu His
 4670 4675 4680

Leu Leu Lys Ser Val Ala Thr Tyr Lys Gly Ile Glu Pro Ser Ala
 4685 4690 4695

Ser Leu Ile Gln Trp Phe Trp Glu Val Met Glu Ser Phe Ser Asn
 4700 4705 4710

Thr Glu Arg Ser Leu Phe Leu Arg Phe Val Trp Gly Arg Thr Arg
 4715 4720 4725

Leu Pro Arg Thr Ile Ala Asp Phe Arg Gly Arg Asp Phe Val Ile
 4730 4735 4740

Gln Val Leu Asp Lys Tyr Asn Pro Pro Asp His Phe Leu Pro Glu
 4745 4750 4755

Ser Tyr Thr Cys Phe Phe Leu Leu Lys Leu Pro Arg Tyr Ser Cys
 4760 4765 4770

Lys Gln Val Leu Glu Glu Lys Leu Lys Tyr Ala Ile His Phe Cys
 4775 4780 4785

Lys Ser Ile Asp Thr Asp Asp Tyr Ala Arg Ile Ala Leu Thr Gly
 4790 4795 4800

Glu Pro Ala Ala Asp Asp Ser Ser Asp Asp Ser Asp Asn Glu Asp
 4805 4810 4815

Val Asp Ser Phe Ala Ser Asp Ser Thr Gln Asp Tyr Leu Thr Gly
 4820 4825 4830

His

<210> 62

<211> 248

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 62

Met Ile Cys Thr Phe Leu Arg Ala Val Gln Tyr Thr Glu Lys Leu His
 1 5 10 15

Arg Ser Ser Ala Lys Arg Leu Leu Leu Pro Tyr Ile Val Leu Asn Lys
 20 25 30

Ala Cys Leu Lys Thr Glu Pro Ser Leu Arg Cys Gly Leu Gln Tyr Gln
 35 40 45

Lys Lys Thr Leu Arg Pro Arg Cys Ile Leu Gly Val Thr Gln Lys Thr
 50 55 60

Ile Trp Thr Gln Gly Pro Ser Pro Arg Lys Ala Lys Glu Asp Gly Ser
 65 70 75 80

Lys Gln Val Ser Val His Arg Ser Gln Arg Gly Gly Thr Ala Val Pro
 85 90 95

Thr Ser Gln Lys Val Lys Glu Ala Gly Arg Asp Phe Thr Tyr Leu Ile
 100 105 110

Val Val Leu Phe Gly Ile Ser Ile Thr Gly Gly Leu Phe Tyr Thr Ile
 115 120 125

Phe Lys Glu Leu Phe Ser Ser Ser Pro Ser Lys Ile Tyr Gly Arg
 130 135 140

Ala Leu Glu Lys Cys Arg Ser His Pro Glu Val Ile Gly Val Phe Gly
 145 150 155 160

Glu Ser Val Lys Gly Tyr Gly Glu Val Thr Arg Arg Gly Arg Arg Gln
 165 170 175

His Val Arg Phe Thr Glu Tyr Val Lys Asp Gly Leu Lys His Thr Cys
 180 185 190

Val Lys Phe Tyr Ile Glu Gly Ser Glu Pro Gly Lys Gln Gly Thr Val
 195 200 205

Tyr Ala Gln Val Lys Glu Asn Pro Gly Ser Gly Glu Tyr Asp Phe Arg
 210 215 220

Tyr Ile Phe Val Glu Ile Glu Ser Tyr Pro Arg Arg Thr Ile Ile Ile
 225 230 235 240

Protein Complexes associated with APP-processing
 Glu Asp Asn Arg Ser Gln Asp Asp
 245

<210> 63

<211> 124

<212> PRT

<213> Homo sapiens

<400> 63

Met Ala Ala Thr Ser Gly Thr Asp Glu Pro Val Ser Gly Glu Leu Val
 1 5 10 15

Ser Val Ala His Ala Leu Ser Leu Pro Ala Glu Ser Tyr Gly Asn Asp
 20 25 30

Pro Asp Ile Glu Met Ala Trp Ala Met Arg Ala Met Gln His Ala Glu
 35 40 45

Val Tyr Tyr Lys Leu Ile Ser Ser Val Asp Pro Gln Phe Leu Lys Leu
 50 55 60

Thr Lys Val Asp Asp Gln Ile Tyr Ser Glu Phe Arg Lys Asn Phe Glu
 65 70 75 80

Thr Leu Arg Ile Asp Val Leu Asp Pro Glu Glu Leu Lys Ser Glu Ser
 85 90 95

Ala Lys Glu Lys Trp Arg Pro Phe Cys Leu Lys Phe Asn Gly Ile Val
 100 105 110

Glu Asp Phe Asn Tyr Gly Thr Leu Leu Arg Leu Asp
 115 120

<210> 64

<211> 1332

<212> PRT

<213> Homo sapiens

<400> 64

Met Arg Asn Leu Lys Leu Phe Arg Thr Leu Glu Phe Arg Asp Ile Gln
 1 5 10 15

Gly Pro Gly Asn Pro Gln Cys Phe Ser Leu Arg Thr Glu Gln Gly Thr
 20 25 30

Protein Complexes associated with APP-processing
 Val Leu Ile Gly Ser Glu His Gly Leu Ile Glu Val Asp Pro Val Ser
 35 40 45

Arg Glu Val Lys Asn Glu Val Ser Leu Val Ala Glu Gly Phe Leu Pro
 50 55 60

Glu Asp Gly Ser Gly Arg Ile Val Gly Val Gln Asp Leu Leu Asp Gln
 65 70 75 80

Glu Ser Val Cys Val Ala Thr Ala Ser Gly Asp Val Ile Leu Cys Ser
 85 90 95

Leu Ser Thr Gln Gln Leu Glu Cys Val Gly Ser Val Ala Ser Gly Ile
 100 105 110

Ser Val Met Ser Trp Ser Pro Asp Gln Glu Leu Val Leu Leu Ala Thr
 115 120 125

Gly Gln Gln Thr Leu Ile Met Met Thr Lys Asp Phe Glu Pro Ile Leu
 130 135 140

Glu Gln Gln Ile His Gln Asp Asp Phe Gly Glu Ser Lys Phe Ile Thr
 145 150 155 160

Val Gly Trp Gly Arg Lys Glu Thr Gln Phe His Gly Ser Glu Gly Arg
 165 170 175

Gln Ala Ala Phe Gln Met Gln Met His Glu Ser Ala Leu Pro Trp Asp
 180 185 190

Asp His Arg Pro Gln Val Thr Trp Arg Gly Asp Gly Gln Phe Phe Ala
 195 200 205

Val Ser Val Val Cys Pro Glu Thr Gly Ala Arg Lys Val Arg Val Trp
 210 215 220

Asn Arg Glu Phe Ala Leu Gln Ser Thr Ser Glu Pro Val Ala Gly Leu
 225 230 235 240

Gly Pro Ala Leu Ala Trp Lys Pro Ser Gly Ser Leu Ile Ala Ser Thr
 245 250 255

Gln Asp Lys Pro Asn Gln Gln Asp Ile Val Phe Phe Glu Lys Asn Gly
 260 265 270

Leu Leu His Gly His Phe Thr Leu Pro Phe Leu Lys Asp Glu Val Lys
 275 280 285

Val Asn Asp Leu Leu Trp Asn Ala Asp Ser Ser Val Leu Ala Val Arg
 290 295 300

Protein Complexes associated with APP-processing

Leu Glu Asp Leu Gln Arg Glu Lys Ser Ser Ile Pro Lys Thr Cys Val
 305 310 315 320

Gln Leu Trp Thr Val Gly Asn Tyr His Trp Tyr Leu Lys Gln Ser Leu
 325 330 335

Ser Phe Ser Thr Cys Gly Lys Ser Lys Ile Val Ser Leu Met Trp Asp
 340 345 350

Pro Val Thr Pro Tyr Arg Leu His Val Leu Cys Gln Gly Trp His Tyr
 355 360 365

Leu Ala Tyr Asp Trp His Trp Thr Thr Asp Arg Ser Val Gly Asp Asn
 370 375 380

Ser Ser Asp Leu Ser Asn Val Ala Val Ile Asp Gly Asn Arg Val Leu
 385 390 395 400

Val Thr Val Phe Arg Gln Thr Val Val Pro Pro Pro Met Cys Thr Tyr
 405 410 415

Gln Leu Leu Phe Pro His Pro Val Asn Gln Val Thr Phe Leu Ala His
 420 425 430

Pro Gln Lys Ser Asn Asp Leu Ala Val Leu Asp Ala Ser Asn Gln Ile
 435 440 445

Ser Val Tyr Lys Cys Gly Asp Cys Pro Ser Ala Asp Pro Thr Val Lys
 450 455 460

Leu Gly Ala Val Gly Gly Ser Gly Phe Lys Val Cys Leu Arg Thr Pro
 465 470 475 480

His Leu Glu Lys Arg Tyr Lys Ile Gln Phe Glu Asn Asn Glu Asp Gln
 485 490 495

Asp Val Asn Pro Leu Lys Leu Gly Leu Leu Thr Trp Ile Glu Glu Asp
 500 505 510

Val Phe Leu Ala Val Ser His Ser Glu Phe Ser Pro Arg Ser Val Ile
 515 520 525

His His Leu Thr Ala Ala Ser Ser Glu Met Asp Glu Glu His Gly Gln
 530 535 540

Leu Asn Val Ser Ser Ser Ala Ala Val Asp Gly Val Ile Ile Ser Leu
 545 550 555 560

Cys Cys Asn Ser Lys Thr Lys Ser Val Val Leu Gln Leu Ala Asp Gly
 565 570 575

Protein Complexes associated with APP-processing
 Gln Ile Phe Lys Tyr Leu Trp Glu Ser Pro Ser Leu Ala Ile Lys Pro
 580 585 590

Trp Lys Asn Ser Gly Gly Phe Pro Val Arg Phe Pro Tyr Pro Cys Thr
 595 600 605

Gln Thr Glu Leu Ala Met Ile Gly Glu Glu Glu Cys Val Leu Gly Leu
 610 615 620

Thr Asp Arg Cys Arg Phe Phe Ile Asn Asp Ile Glu Val Ala Ser Asn
 625 630 635 640

Ile Thr Ser Phe Ala Val Tyr Asp Glu Phe Leu Leu Leu Thr Thr His
 645 650 655

Ser His Thr Cys Gln Cys Phe Cys Leu Arg Asp Ala Ser Phe Lys Thr
 660 665 670

Leu Gln Ala Gly Leu Ser Ser Asn His Val Ser His Gly Glu Val Leu
 675 680 685

Arg Lys Val Glu Arg Gly Ser Arg Ile Val Thr Val Val Pro Gln Asp
 690 695 700

Thr Lys Leu Val Leu Gln Met Pro Arg Gly Asn Leu Glu Val Val His
 705 710 715 720

His Arg Ala Leu Val Leu Ala Gln Ile Arg Lys Trp Leu Asp Lys Leu
 725 730 735

Met Phe Lys Glu Ala Phe Glu Cys Met Arg Lys Leu Arg Ile Asn Leu
 740 745 750

Asn Pro Ile Tyr Asp His Asn Pro Lys Val Phe Leu Gly Asn Val Glu
 755 760 765

Thr Phe Ile Lys Gln Ile Asp Ser Val Asn His Ile Asn Leu Phe Phe
 775 780

Thr Glu Leu Lys Glu Glu Asp Val Thr Lys Thr Met Tyr Pro Ala Pro
 785 790 795 800

Val Thr Ser Ser Val Tyr Leu Ser Arg Asp Pro Asp Gly Asn Lys Ile
 805 810 815

Asp Leu Val Cys Asp Ala Met Arg Ala Val Met Glu Ser Ile Asn Pro
 820 825 830

His Lys Tyr Cys Leu Ser Ile Leu Thr Ser His Val Lys Lys Thr Thr
 835 840 845

Protein Complexes associated with APP-processing
 Pro Glu Leu Glu Ile Val Leu Gln Lys Val His Glu Leu Gln Gly Asn
 850 855 860

Ala Pro Ser Asp Pro Asp Ala Val Ser Ala Glu Glu Ala Leu Lys Tyr
 865 870 875 880

Leu Leu His Leu Val Asp Val Asn Glu Leu Tyr Asp His Ser Leu Gly
 885 890 895

Thr Tyr Asp Phe Asp Leu Val Leu Met Val Ala Glu Lys Ser Gln Lys
 900 905 910

Asp Pro Lys Glu Tyr Leu Pro Phe Leu Asn Thr Leu Lys Lys Met Glu
 915 920 925

Thr Asn Tyr Gln Arg Phe Thr Ile Asp Lys Tyr Leu Lys Arg Tyr Glu
 930 935 940

Lys Ala Ile Gly His Leu Ser Lys Cys Gly Pro Glu Tyr Phe Pro Glu
 945 950 955 960

Cys Leu Asn Leu Ile Lys Asp Lys Asn Leu Tyr Asn Glu Ala Leu Lys
 965 970 975

Leu Tyr Ser Pro Ser Ser Gln Gln Tyr Gln Asp Ile Ser Ile Ala Tyr
 980 985 990

Gly Glu His Leu Met Gln Glu His Met Tyr Glu Pro Ala Gly Leu Met
 995 1000 1005

Phe Ala Arg Cys Gly Ala His Glu Lys Ala Leu Ser Ala Phe Leu
 1010 1015 1020

Thr Cys Gly Asn Trp Lys Gln Ala Leu Cys Val Ala Ala Gln Leu
 1025 1030 1035

Asn Phe Thr Lys Asp Gln Leu Val Gly Leu Gly Arg Thr Leu Ala
 1040 1045 1050

Gly Lys Leu Val Glu Gln Arg Lys His Ile Asp Ala Ala Met Val
 1055 1060 1065

Leu Glu Glu Ser Ala Gln Asp Tyr Glu Glu Ala Val Leu Leu Leu
 1070 1075 1080

Leu Glu Gly Ala Ala Trp Glu Glu Ala Leu Arg Leu Val Tyr Lys
 1085 1090 1095

Tyr Asn Arg Leu Asp Ile Ile Glu Thr Asn Val Lys Pro Ser Ile
 1100 1105 1110

Protein Complexes associated with APP-processing

Leu Glu Ala Gln Lys Asn Tyr Met Ala Phe Leu Asp Ser Gln Thr
 1115 1120 1125

Ala Thr Phe Ser Arg His Lys Lys Arg Leu Leu Val Val Arg Glu
 1130 1135 1140

Leu Lys Glu Gln Ala Gln Gln Ala Gly Leu Asp Asp Glu Val Pro
 1145 1150 1155

His Gly Gln Glu Ser Asp Leu Phe Ser Glu Thr Ser Ser Val Val
 1160 1165 1170

Ser Gly Ser Glu Met Ser Gly Lys Tyr Ser His Ser Asn Ser Arg
 1175 1180 1185

Ile Ser Ala Arg Ser Ser Lys Asn Arg Arg Lys Ala Glu Arg Lys
 1190 1195 1200

Lys His Ser Leu Lys Glu Gly Ser Pro Leu Glu Asp Leu Ala Leu
 1205 1210 1215

Leu Glu Ala Leu Ser Glu Val Val Gln Asn Thr Glu Asn Leu Lys
 1220 1225 1230

Asp Glu Val Tyr His Ile Leu Lys Val Leu Phe Leu Phe Glu Phe
 1235 1240 1245

Asp Glu Gln Gly Arg Glu Leu Gln Lys Ala Phe Glu Asp Thr Leu
 1250 1255 1260

Gln Leu Met Glu Arg Ser Leu Pro Glu Ile Trp Thr Leu Thr Tyr
 1265 1270 1275

Gln Gln Asn Ser Ala Thr Pro Val Leu Gly Pro Asn Ser Thr Ala
 1280 1285 1290

Asn Ser Ile Met Ala Ser Tyr Gln Gln Gln Lys Thr Ser Val Pro
 1295 1300 1305

Val Leu Asp Ala Glu Leu Phe Ile Pro Pro Lys Ile Asn Arg Arg
 1310 1315 1320

Thr Gln Trp Lys Leu Ser Leu Leu Asp
 1325 1330

<210> 65

<211> 1647

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 65

Met Val Gln Lys Lys Lys Phe Cys Pro Arg Leu Leu Asp Tyr Leu Val
 1 5 10 15

Ile Val Gly Ala Arg His Pro Ser Ser Asp Ser Val Ala Gln Thr Pro
 20 25 30

Glu Leu Leu Arg Arg Tyr Pro Leu Glu Asp His Thr Glu Phe Pro Leu
 35 40 45

Pro Pro Asp Val Val Phe Phe Cys Gln Pro Glu Gly Cys Leu Ser Val
 50 55 60

Arg Gln Arg Arg Met Ser Leu Arg Asp Asp Thr Ser Phe Val Phe Thr
 65 70 75 80

Leu Thr Asp Lys Asp Thr Gly Val Thr Arg Tyr Gly Ile Cys Val Asn
 85 90 95

Phe Tyr Arg Ser Phe Gln Lys Arg Ile Ser Lys Gly Lys Gly Glu Gly
 100 105 110

Gly Ala Gly Ser Arg Gly Lys Glu Gly Thr His Ala Thr Cys Ala Ser
 115 120 125

Glu Glu Gly Gly Thr Glu Ser Ser Glu Ser Gly Ser Ser Leu Gln Pro
 130 135 140

Phe Ser Ala Asp Ser Thr Pro Asp Val Asn Gln Ser Pro Arg Gly Lys
 145 150 155 160

Arg Arg Ala Lys Ala Gly Ser Arg Ser Arg Asn Ser Thr Leu Thr Ser
 165 170 175

Leu Cys Val Leu Ser His Tyr Pro Phe Phe Ser Thr Phe Arg Glu Cys
 180 185 190

Leu Tyr Thr Leu Lys Arg Leu Val Asp Cys Cys Ser Glu Arg Leu Leu
 195 200 205

Gly Lys Lys Leu Gly Ile Pro Arg Gly Val Gln Arg Asp Thr Met Trp
 210 215 220

Arg Ile Phe Thr Gly Ser Leu Leu Val Glu Glu Lys Ser Ser Ala Leu
 225 230 235 240

Leu His Asp Leu Arg Glu Ile Glu Ala Trp Ile Tyr Arg Leu Leu Arg
 245 250 255

Protein Complexes associated with APP-processing

Ser Pro Val Pro Val Ser Gly Gln Lys Arg Val Asp Ile Glu Val Leu
 260 265 270

Pro Gln Glu Leu Gln Pro Ala Leu Thr Phe Ala Leu Pro Asp Pro Ser
 275 280 285

Arg Phe Thr Leu Val Asp Phe Pro Leu His Leu Pro Leu Glu Leu Leu
 290 295 300

Gly Val Asp Ala Cys Leu Gln Leu Leu Thr Cys Ile Leu Leu Glu His
 305 310 315 320

Lys Val Val Leu Gln Ser Arg Asp Tyr Asn Ala Leu Ser Met Ser Val
 325 330 335

Met Ala Phe Val Ala Met Ile Tyr Pro Leu Glu Tyr Met Phe Pro Val
 340 345 350

Ile Pro Leu Leu Pro Thr Cys Met Ala Ser Ala Glu Gln Leu Leu Leu
 355 360 365

Ala Pro Thr Pro Tyr Ile Ile Gly Val Pro Ala Ser Phe Phe Leu Tyr
 370 375 380

Lys Leu Asp Phe Lys Met Pro Asp Asp Val Trp Leu Val Asp Leu Asp
 385 390 395 400

Ser Asn Arg Val Ile Ala Pro Thr Asn Ala Glu Val Leu Pro Ile Leu
 405 410 415

Pro Glu Pro Glu Ser Leu Glu Leu Lys Lys His Leu Lys Gln Ala Leu
 420 425 430

Ala Ser Met Ser Leu Asn Thr Gln Pro Ile Leu Asn Leu Glu Lys Phe
 435 440 445

His Glu Gly Gln Glu Ile Pro Leu Leu Leu Gly Arg Pro Ser Asn Asp
 450 455 460

Leu Gln Ser Thr Pro Ser Thr Glu Phe Asn Pro Leu Ile Tyr Gly Asn
 465 470 475 480

Asp Ala Asp Ser Val Asp Val Ala Thr Arg Val Ala Met Val Arg Phe
 485 490 495

Phe Asn Ser Ala Asn Val Leu Gln Gly Phe Gln Met His Thr Arg Thr
 500 505 510

Leu Arg Leu Phe Pro Arg Pro Val Val Ala Phe Gln Ala Gly Ser Phe
 515 520 525

Protein Complexes associated with APP-processing

Leu Ala Ser Arg Pro Arg Gln Thr Pro Phe Ala Glu Lys Leu Ala Arg
 530 535 540

Thr Gln Ala Val Glu Tyr Phe Gly Glu Trp Ile Leu Asn Pro Thr Asn
 545 550 555 560

Tyr Ala Phe Gln Arg Ile His Asn Asn Met Phe Asp Pro Ala Leu Ile
 565 570 575

Gly Asp Lys Pro Lys Trp Tyr Ala His Gln Leu Gln Pro Ile His Tyr
 580 585 590

Arg Val Tyr Asp Ser Asn Ser Gln Leu Ala Glu Ala Leu Ser Val Pro
 595 600 605

Pro Glu Arg Asp Ser Asp Ser Glu Pro Thr Asp Asp Ser Gly Ser Asp
 610 615 620

Ser Met Asp Tyr Asp Asp Ser Ser Ser Ser Tyr Ser Ser Leu Gly Asp
 625 630 635 640

Phe Val Ser Glu Met Met Lys Cys Asp Ile Asn Gly Asp Thr Pro Asn
 645 650 655

Val Asp Pro Leu Thr His Ala Ala Leu Gly Asp Ala Ser Glu Val Glu
 660 665 670

Ile Asp Glu Leu Gln Asn Gln Lys Glu Ala Glu Glu Pro Gly Pro Asp
 675 680 685

Ser Glu Asn Ser Gln Glu Asn Pro Pro Leu Arg Ser Ser Ser Ser Thr
 690 695 700

Thr Ala Ser Ser Ser Pro Ser Thr Val Ile His Gly Ala Asn Ser Glu
 705 710 715 720

Pro Ala Asp Ser Thr Glu Met Asp Asp Lys Ala Ala Val Gly Val Ser
 725 730 735

Lys Pro Leu Pro Ser Val Pro Pro Ser Ile Gly Lys Ser Asn Val Asp
 740 745 750

Arg Arg Gln Ala Glu Ile Gly Glu Gly Ser Val Arg Arg Arg Ile Tyr
 755 760 765

Asp Asn Pro Tyr Phe Glu Pro Gln Tyr Gly Phe Pro Pro Glu Glu Asp
 770 775 780

Glu Asp Glu Gln Gly Glu Ser Tyr Thr Pro Arg Phe Ser Gln His Val
 785 790 795 800

Protein Complexes associated with APP-processing

Ser Gly Asn Arg Ala Gln Lys Leu Leu Arg Pro Asn Ser Leu Arg Leu
805 810 815

Ala Ser Asp Ser Asp Ala Glu Ser Asp Ser Arg Ala Ser Ser Pro Asn
820 825 830

Ser Thr Val Ser Asn Thr Ser Thr Glu Gly Phe Gly Gly Ile Met Ser
835 840 845

Phe Ala Ser Ser Leu Tyr Arg Asn His Ser Thr Ser Phe Ser Leu Ser
850 855 860

Asn Leu Thr Leu Pro Thr Lys Gly Ala Arg Glu Lys Ala Thr Pro Phe
865 870 875 880

Pro Ser Leu Lys Val Phe Gly Leu Asn Thr Leu Met Glu Ile Val Thr
885 890 895

Glu Ala Gly Pro Gly Ser Gly Glu Gly Asn Arg Arg Ala Leu Val Asp
900 905 910

Gln Lys Ser Ser Val Ile Lys His Ser Pro Thr Val Lys Arg Glu Pro
915 920 925

Pro Ser Pro Gln Gly Arg Ser Ser Asn Ser Ser Glu Asn Gln Gln Phe
930 935 940

Leu Lys Glu Val Val His Ser Val Leu Asp Gly Gln Gly Val Gly Trp
945 950 955 960

Leu Asn Met Lys Lys Val Arg Arg Leu Leu Glu Ser Glu Gln Leu Arg
965 970 975

Val Phe Val Leu Ser Lys Leu Asn Arg Met Val Gln Ser Glu Asp Asp
980 985 990

Ala Arg Gln Asp Ile Ile Pro Asp Val Glu Ile Ser Arg Lys Val Tyr
995 1000 1005

Lys Gly Met Leu Asp Leu Leu Lys Cys Thr Val Leu Ser Leu Glu
1010 1015 1020

Gln Ser Tyr Ala His Ala Gly Leu Gly Gly Met Ala Ser Ile Phe
1025 1030 1035

Gly Leu Leu Glu Ile Ala Gln Thr His Tyr Tyr Ser Lys Glu Pro
1040 1045 1050

Asp Lys Arg Lys Arg Ser Pro Thr Glu Ser Val Asn Thr Pro Val
1055 1060 1065

Protein Complexes associated with APP-processing

Gly	Lys	Asp	Pro	Gly	Leu	Ala	Gly	Arg	Gly	Asp	Pro	Lys	Ala	Met
	1070					1075					1080			
Ala	Gln	Leu	Arg	Val	Pro	Gln	Leu	Gly	Pro	Arg	Ala	Pro	Ser	Ala
	1085					1090					1095			
Thr	Gly	Lys	Gly	Pro	Lys	Glu	Leu	Asp	Thr	Arg	Ser	Leu	Lys	Glu
	1100					1105					1110			
Glu	Asn	Phe	Ile	Ala	Ser	Ile	Glu	Leu	Trp	Asn	Lys	His	Gln	Glu
	1115					1120					1125			
Val	Lys	Lys	Gln	Lys	Ala	Leu	Glu	Lys	Gln	Arg	Pro	Glu	Val	Ile
	1130					1135					1140			
Lys	Pro	Val	Phe	Asp	Leu	Gly	Glu	Thr	Glu	Glu	Lys	Lys	Ser	Gln
	1145					1150					1155			
Ile	Ser	Ala	Asp	Ser	Gly	Val	Ser	Leu	Thr	Ser	Ser	Ser	Gln	Arg
	1160					1165					1170			
Thr	Asp	Gln	Asp	Ser	Val	Ile	Gly	Val	Ser	Pro	Ala	Val	Met	Ile
	1175					1180					1185			
Arg	Ser	Ser	Ser	Gln	Asp	Ser	Glu	Val	Ser	Thr	Val	Val	Ser	Asn
	1190					1195					1200			
Ser	Ser	Gly	Glu	Thr	Leu	Gly	Ala	Asp	Ser	Asp	Leu	Ser	Ser	Asn
	1205					1210					1215			
Ala	Gly	Asp	Gly	Pro	Gly	Gly	Glu	Gly	Ser	Val	His	Leu	Ala	Ser
	1220					1225					1230			
Ser	Arg	Gly	Thr	Leu	Ser	Asp	Ser	Glu	Ile	Glu	Thr	Asn	Ser	Ala
	1235					1240					1245			
Thr	Ser	Thr	Ile	Phe	Gly	Lys	Ala	His	Ser	Leu	Lys	Pro	Cys	Ile
	1250					1255					1260			
Lys	Glu	Lys	Leu	Ala	Gly	Ser	Pro	Ile	Arg	Thr	Ser	Glu	Asp	Val
	1265					1270					1275			
Ser	Gln	Arg	Val	Tyr	Leu	Tyr	Glu	Gly	Leu	Leu	Gly	Arg	Asp	Lys
	1280					1285					1290			
Gly	Ser	Met	Trp	Asp	Gln	Leu	Glu	Asp	Ala	Ala	Met	Glu	Thr	Phe
	1295					1300					1305			
Ser	Ile	Ser	Lys	Glu	Arg	Ser	Thr	Leu	Trp	Asp	Gln	Met	Gln	Phe
	1310					1315					1320			

Protein Complexes associated with APP-processing

Trp	Glu	Asp	Ala	Phe	Leu	Asp	Ala	Val	Met	Leu	Glu	Arg	Glu	Gly
	1325					1330					1335			
Met	Gly	Met	Asp	Gln	Gly	Pro	Gln	Glu	Met	Ile	Asp	Arg	Tyr	Leu
	1340					1345					1350			
Ser	Leu	Gly	Glu	His	Asp	Arg	Lys	Arg	Leu	Glu	Asp	Asp	Glu	Asp
	1355					1360					1365			
Arg	Leu	Leu	Ala	Thr	Leu	Leu	His	Asn	Leu	Ile	Ser	Tyr	Met	Leu
	1370					1375					1380			
Leu	Met	Lys	Val	Asn	Lys	Asn	Asp	Ile	Arg	Lys	Lys	Val	Arg	Arg
	1385					1390					1395			
Leu	Met	Gly	Lys	Ser	His	Ile	Gly	Leu	Val	Tyr	Ser	Gln	Gln	Ile
	1400					1405					1410			
Asn	Glu	Val	Leu	Asp	Gln	Leu	Ala	Asn	Leu	Asn	Gly	Arg	Asp	Leu
	1415					1420					1425			
Ser	Ile	Trp	Ser	Ser	Gly	Ser	Arg	His	Met	Lys	Lys	Gln	Thr	Phe
	1430					1435					1440			
Val	Val	His	Ala	Gly	Thr	Asp	Thr	Asn	Gly	Asp	Ile	Phe	Phe	Met
	1445					1450					1455			
Glu	Val	Cys	Asp	Asp	Cys	Val	Val	Leu	Arg	Ser	Asn	Ile	Gly	Thr
	1460					1465					1470			
Val	Tyr	Glu	Arg	Trp	Trp	Tyr	Glu	Lys	Leu	Ile	Asn	Met	Thr	Tyr
	1475					1480					1485			
Cys	Pro	Lys	Thr	Lys	Val	Leu	Cys	Leu	Trp	Arg	Arg	Asn	Gly	Ser
	1490					1495					1500			
Glu	Thr	Gln	Leu	Asn	Lys	Phe	Tyr	Thr	Lys	Lys	Cys	Arg	Glu	Leu
	1505					1510					1515			
Tyr	Tyr	Cys	Val	Lys	Asp	Ser	Met	Glu	Arg	Ala	Ala	Ala	Arg	Gln
	1520					1525					1530			
Gln	Ser	Ile	Lys	Pro	Gly	Pro	Glu	Leu	Gly	Gly	Glu	Phe	Pro	Val
	1535					1540					1545			
Gln	Asp	Leu	Lys	Thr	Gly	Glu	Gly	Gly	Leu	Leu	Gln	Val	Thr	Leu
	1550					1555					1560			
Glu	Gly	Ile	Asn	Leu	Lys	Phe	Met	His	Asn	Gln	Val	Phe	Ile	Glu
	1565					1570					1575			

Protein Complexes associated with APP-processing

Leu Asn His Ile Lys Lys Cys Asn Thr Val Arg Gly Val Phe Val
 1580 1585 1590

Leu Glu Glu Phe Val Pro Glu Ile Lys Glu Val Val Ser His Lys
 1595 1600 1605

Tyr Lys Thr Pro Met Ala His Glu Ile Cys Tyr Ser Val Leu Cys
 1610 1615 1620

Leu Phe Ser Tyr Val Ala Ala Val His Ser Ser Glu Glu Asp Leu
 1625 1630 1635

Arg Thr Pro Pro Arg Pro Val Ser Ser
 1640 1645

<210> 66

<211> 1507

<212> PRT

<213> Homo sapiens

<400> 66

Ala Ala Ala Ser Arg Cys Pro Gly Ile Met Val Ala Leu Arg Gly Leu
 1 5 10 15

Gly Ser Gly Leu Gln Pro Trp Cys Pro Leu Asp Leu Arg Leu Glu Trp
 20 25 30

Val Asp Thr Val Trp Glu Leu Asp Phe Thr Glu Thr Glu Pro Leu Asp
 35 40 45

Pro Ser Ile Glu Ala Glu Ile Ile Glu Thr Gly Leu Ala Ala Phe Thr
 50 55 60

Lys Leu Tyr Glu Ser Leu Leu Pro Phe Ala Thr Gly Glu His Gly Ser
 65 70 75 80

Met Glu Ser Ile Trp Thr Phe Phe Ile Glu Asn Asn Val Ser His Ser
 85 90 95

Thr Leu Val Ala Leu Phe Tyr His Phe Val Gln Ile Val His Lys Lys
 100 105 110

Asn Val Ser Val Gln Tyr Arg Glu Tyr Gly Leu His Ala Ala Gly Leu
 115 120 125

Tyr Phe Leu Leu Leu Glu Val Pro Gly Ser Val Ala Asn Gln Val Phe
 130 135 140

Protein Complexes associated with APP-processing

His Pro Val Met Phe Asp Lys Cys Ile Gln Thr Leu Lys Lys Ser Trp
 145 150 155 160

Pro Gln Glu Ser Asn Leu Asn Arg Lys Arg Lys Lys Glu Gln Pro Lys
 165 170 175

Ser Ser Gln Ala Asn Pro Gly Arg His Arg Lys Arg Gly Lys Pro Pro
 180 185 190

Arg Arg Glu Asp Ile Glu Met Asp Glu Ile Ile Glu Glu Gln Glu Asp
 195 200 205

Glu Asn Ile Cys Phe Ser Ala Arg Asp Leu Ser Gln Ile Arg Asn Ala
 210 215 220

Ile Phe His Leu Leu Lys Asn Phe Leu Arg Leu Leu Pro Lys Phe Ser
 225 230 235 240

Leu Lys Glu Lys Pro Gln Cys Val Gln Asn Cys Ile Glu Val Phe Val
 245 250 255

Ser Leu Thr Asn Phe Glu Pro Val Leu His Glu Cys His Val Thr Gln
 260 265 270

Ala Arg Ala Leu Asn Gln Ala Lys Tyr Ile Pro Glu Leu Ala Tyr Tyr
 275 280 285

Gly Leu Tyr Leu Leu Cys Ser Pro Ile His Gly Glu Gly Asp Lys Val
 290 295 300

Ile Ser Cys Val Phe His Gln Met Leu Ser Val Ile Leu Met Leu Glu
 305 310 315 320

Val Gly Glu Gly Ser His Arg Ala Pro Leu Ala Val Thr Ser Gln Val
 325 330 335

Ile Asn Cys Arg Asn Gln Ala Val Gln Phe Ile Ser Ala Leu Val Asp
 340 345 350

Glu Leu Lys Glu Ser Ile Phe Pro Val Val Arg Ile Leu Leu Gln His
 355 360 365

Ile Cys Ala Lys Val Val Asp Lys Ser Glu Tyr Arg Thr Phe Ala Ala
 370 375 380

Gln Ser Leu Val Gln Leu Leu Ser Lys Leu Pro Cys Gly Glu Tyr Ala
 385 390 395 400

Met Phe Ile Ala Trp Leu Tyr Lys Tyr Ser Arg Ser Ser Lys Ile Pro
 405 410 415

Protein Complexes associated with APP-processing

His Arg Val Phe Thr Leu Asp Val Val Leu Ala Leu Leu Glu Leu Pro
420 425 430

Glu Arg Glu Val Asp Asn Thr Leu Ser Leu Glu His Gln Lys Phe Leu
435 440 445

Lys His Lys Phe Leu Val Gln Glu Ile Met Phe Asp Arg Cys Leu Asp
450 455 460

Lys Ala Pro Thr Val Arg Ser Lys Ala Leu Ser Ser Phe Ala His Cys
465 470 475 480

Leu Glu Leu Thr Val Thr Ser Ala Ser Glu Ser Ile Leu Glu Leu Leu
485 490 495

Ile Asn Ser Pro Thr Phe Ser Val Ile Glu Ser His Pro Gly Thr Leu
500 505 510

Leu Arg Asn Ser Ser Ala Phe Ser Tyr Gln Arg Gln Thr Ser Asn Arg
515 520 525

Ser Glu Pro Ser Gly Glu Ile Asn Ile Asp Ser Ser Gly Glu Thr Val
530 535 540

Gly Ser Gly Glu Arg Cys Val Met Ala Met Leu Arg Arg Arg Ile Arg
545 550 555 560

Asp Glu Lys Thr Asn Val Arg Lys Ser Ala Leu Gln Val Leu Val Ser
565 570 575

Ile Leu Lys His Cys Asp Val Ser Gly Met Lys Glu Asp Leu Trp Ile
580 585 590

Leu Gln Asp Gln Cys Arg Asp Pro Ala Val Ser Val Arg Lys Gln Ala
595 600 605

Leu Gln Ser Leu Thr Glu Leu Leu Met Ala Gln Pro Arg Cys Val Gln
610 615 620

Ile Gln Lys Ala Trp Leu Arg Gly Val Val Pro Val Val Met Asp Cys
625 630 635 640

Glu Ser Thr Val Gln Glu Lys Ala Leu Glu Phe Leu Asp Gln Leu Leu
645 650 655

Leu Gln Asn Ile Arg His His Ser His Phe His Ser Gly Asp Asp Ser
660 665 670

Gln Val Leu Ala Trp Ala Leu Leu Thr Leu Leu Thr Thr Glu Ser Gln
675 680 685

Protein Complexes associated with APP-processing
 Glu Leu Ser Arg Tyr Leu Asn Lys Ala Phe His Ile Trp Ser Lys Lys
 690 695 700

Glu Lys Phe Ser Pro Thr Phe Ile Asn Asn Val Ile Ser His Thr Gly
 705 710 715 720

Thr Glu His Ser Ala Pro Ala Trp Met Leu Leu Ser Lys Ile Ala Gly
 725 730 735

Ser Ser Pro Arg Leu Asp Tyr Ser Arg Ile Ile Gln Ser Trp Glu Lys
 740 745 750

Ile Ser Ser Gln Gln Asn Pro Asn Ser Asn Thr Leu Gly His Ile Leu
 755 760 765

Cys Val Ile Gly His Ile Ala Lys His Leu Pro Lys Ser Thr Arg Asp
 770 775 780

Lys Val Thr Asp Ala Val Lys Cys Lys Leu Asn Gly Phe Gln Trp Ser
 785 790 795 800

Leu Glu Val Ile Ser Ser Ala Val Asp Ala Leu Gln Arg Leu Cys Arg
 805 810 815

Ala Ser Ala Glu Thr Pro Ala Glu Glu Gln Glu Leu Leu Thr Gln Val
 820 825 830

Cys Gly Asp Val Leu Ser Thr Cys Glu His Arg Leu Ser Asn Ile Val
 835 840 845

Leu Lys Glu Asn Gly Thr Gly Asn Met Asp Glu Asp Leu Leu Val Lys
 850 855 860

Tyr Ile Phe Thr Leu Gly Asp Ile Ala Gln Leu Cys Pro Ala Arg Val
 865 870 875 880

Glu Lys Arg Ile Phe Leu Leu Ile Gln Ser Val Leu Ala Ser Ser Ala
 885 890 895

Asp Ala Asp His Ser Pro Ser Ser Gln Gly Ser Ser Glu Ala Pro Ala
 900 905 910

Ser Gln Pro Pro Pro Gln Val Arg Gly Ser Val Met Pro Ser Val Ile
 915 920 925

Arg Ala His Ala Ile Ile Thr Leu Gly Lys Leu Cys Leu Gln His Glu
 930 935 940

Asp Leu Ala Lys Lys Ser Ile Pro Ala Leu Val Arg Glu Leu Glu Val
 945 950 955 960

Protein Complexes associated with APP-processing
Cys Glu Asp Val Ala Val Arg Asn Asn Val Ile Ile Val Met Cys Asp
965 970 975

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Protein Complexes associated with APP-processing

Thr Val Leu Glu Lys Asn Lys Ile Pro Ala Leu Arg Glu Leu Met
 1220 1225 1230

His Tyr Leu Arg Glu Val Met Gln Asp Tyr Arg Asp Glu Leu Lys
 1235 1240 1245

Asp Phe Phe Ala Val Asp Lys Gln Leu Ala Ser Glu Leu Glu Tyr
 1250 1255 1260

Asp Met Lys Lys Tyr Gln Glu Gln Leu Val Gln Glu Gln Glu Leu
 1265 1270 1275

Ala Lys His Ala Asp Val Ala Gly Thr Ala Gly Gly Ala Glu Val
 1280 1285 1290

Ala Pro Val Ala Gln Val Ala Leu Cys Leu Glu Thr Val Pro Val
 1295 1300 1305

Pro Ala Gly Gln Glu Asn Pro Ala Met Ser Pro Ala Val Ser Gln
 1310 1315 1320

Pro Cys Thr Pro Arg Ala Ser Ala Gly His Val Ala Val Ser Ser
 1325 1330 1335

Pro Thr Pro Glu Thr Gly Pro Leu Gln Arg Leu Leu Pro Lys Ala
 1340 1345 1350

Arg Pro Met Ser Leu Ser Thr Ile Ala Ile Leu Asn Ser Val Lys
 1355 1360 1365

Lys Ala Val Glu Ser Lys Ser Arg His Arg Ser Arg Ser Leu Gly
 1370 1375 1380

Val Leu Pro Phe Thr Leu Asn Ser Gly Ser Pro Glu Lys Thr Cys
 1385 1390 1395

Ser Gln Val Ser Ser Tyr Ser Leu Glu Gln Glu Ser Asn Gly Glu
 1400 1405 1410

Ile Glu His Val Thr Lys Arg Ala Ile Ser Thr Pro Glu Lys Ser
 1415 1420 1425

Ile Ser Asp Val Thr Phe Gly Ala Gly Val Ser Tyr Ile Gly Thr
 1430 1435 1440

Pro Arg Thr Pro Ser Ser Ala Lys Glu Lys Ile Glu Gly Arg Ser
 1445 1450 1455

Gln Gly Asn Asp Ile Leu Cys Leu Ser Leu Pro Asp Lys Pro Pro
 1460 1465 1470

Protein Complexes associated with APP-processing
 Pro Gln Pro Gln Gln Trp Asn Val Arg Ser Pro Ala Arg Asn Lys
 1475 1480 1485

Asp Thr Pro Ala Cys Ser Arg Arg Ser Leu Arg Lys Thr Pro Leu
 1490 1495 1500

Lys Thr Ala Asn
 1505

<210> 67

<211> 2209

<212> PRT

<213> Homo sapiens

<400> 67

Met Trp Asn Asp Ile Glu Leu Leu Thr Asn Asp Asp Thr Gly Ser Gly
 1 5 10 15

Tyr Leu Ser Val Gly Ser Arg Lys Glu His Gly Thr Ala Leu Tyr Gln
 20 25 30

Val Asp Leu Leu Val Lys Ile Ser Ser Glu Lys Ala Ser Leu Asn Pro
 35 40 45

Lys Ile Gln Ala Cys Ser Leu Ser Asp Gly Phe Ile Ile Val Ala Asp
 50 55 60

Gln Ser Val Ile Leu Leu Asp Ser Ile Cys Arg Ser Leu Gln Leu His
 65 70 75 80

Leu Val Phe Asp Thr Glu Val Asp Val Val Gly Leu Cys Gln Glu Gly
 85 90 95

Lys Phe Leu Leu Val Gly Glu Arg Ser Gly Asn Leu His Leu Ile His
 100 105 110

Val Thr Ser Lys Gln Thr Leu Leu Thr Asn Ala Phe Val Gln Lys Ala
 115 120 125

Asn Asp Glu Asn Arg Arg Thr Tyr Gln Asn Leu Val Ile Glu Lys Asp
 130 135 140

Gly Ser Asn Glu Gly Thr Tyr Tyr Met Leu Leu Leu Thr Tyr Ser Gly
 145 150 155 160

Phe Phe Cys Ile Thr Asn Leu Gln Leu Leu Lys Ile Gln Gln Ala Ile
 165 170 175

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Protein Complexes associated with APP-processing

Thr Glu Trp Gln Gln Leu Val Asp Asp Ala Lys Glu Asn Leu His Lys
450 455 460

Ile Gln Asp Asp Glu Phe Val Val Asn Tyr Cys Leu Lys Ala Gln Trp
465 470 475 480

Ile Thr Tyr Glu Thr Thr Gln Glu Met Leu Asn Tyr Ala Lys Thr Arg
485 490 495

Leu Leu Lys Lys Glu Asp Lys Thr Ala Leu Ile Tyr Ser Asp Gly Leu
500 505 510

Lys Glu Val Leu Arg Ala His Ala Lys Leu Thr Thr Phe Tyr Gly Ala
515 520 525

Phe Gly Pro Glu Lys Phe Ser Gly Ser Ser Trp Ile Glu Phe Leu Asn
530 535 540

Asn Glu Asp Asp Leu Lys Asp Ile Phe Leu Gln Leu Lys Glu Gly Asn
545 550 555 560

Leu Val Cys Ala Gln Tyr Leu Trp Leu Arg His Arg Ala Asn Phe Glu
565 570 575

Ser Arg Phe Asp Val Lys Met Leu Glu Ser Leu Leu Asn Ser Met Ser
580 585 590

Ala Ser Val Ser Leu Gln Lys Leu Cys Pro Trp Phe Lys Asn Asp Val
595 600 605

Ile Pro Phe Val Arg Arg Thr Val Pro Glu Gly Gln Ile Ile Leu Ala
610 615 620

Lys Trp Leu Glu Gln Ala Ala Arg Asn Leu Glu Leu Thr Asp Lys Ala
625 630 635 640

Asn Trp Pro Glu Asn Gly Leu Gln Leu Ala Glu Ile Phe Phe Thr Ala
645 650 655

Glu Lys Thr Asp Glu Leu Gly Leu Ala Ser Ser Trp His Trp Ile Ser
660 665 670

Leu Lys Asp Tyr Gln Asn Thr Glu Glu Val Cys Gln Leu Arg Thr Leu
675 680 685

Val Asn Asn Leu Arg Glu Leu Ile Thr Leu His Arg Lys Tyr Asn Cys
690 695 700

Lys Leu Ala Leu Ser Asp Phe Glu Lys Glu Asn Thr Thr Thr Ile Val
705 710 715 720

Protein Complexes associated with APP-processing

Phe Arg Met Phe Asp Lys Val Leu Ala Pro Glu Leu Ile Pro Ser Ile
725 730 735

Leu Glu Lys Phe Ile Arg Val Tyr Met Arg Glu His Asp Leu Gln Glu
740 745 750

Glu Glu Leu Leu Leu Leu Tyr Ile Glu Asp Leu Leu Asn Arg Cys Ser
755 760 765

Ser Lys Ser Thr Ser Leu Phe Glu Thr Ala Trp Glu Ala Lys Ala Met
770 775 780

Ala Val Ile Ala Cys Leu Ser Asp Thr Asp Leu Ile Phe Asp Ala Val
785 790 795 800

Leu Lys Ile Met Tyr Ala Ala Val Val Pro Trp Ser Ala Ala Val Glu
805 810 815

Gln Leu Val Lys Gln His Leu Glu Met Asp His Pro Lys Val Lys Leu
820 825 830

Leu Gln Glu Ser Tyr Lys Leu Met Glu Met Lys Lys Leu Leu Arg Gly
835 840 845

Tyr Gly Ile Arg Glu Val Asn Leu Leu Asn Lys Glu Ile Met Arg Val
850 855 860

Val Arg Tyr Ile Leu Lys Gln Asp Val Pro Ser Ser Leu Glu Asp Ala
865 870 875 880

Leu Lys Val Ala Gln Ala Phe Met Leu Ser Asp Asp Glu Ile Tyr Ser
885 890 895

Leu Arg Ile Ile Asp Leu Ile Asp Arg Glu Gln Gly Glu Asp Cys Leu
900 905 910

Leu Leu Leu Lys Ser Leu Pro Pro Ala Glu Ala Glu Lys Thr Ala Glu
915 920 925

Arg Val Ile Ile Trp Ala Arg Leu Ala Leu Gln Glu Glu Pro Asp His
930 935 940

Ser Lys Glu Gly Lys Ala Trp Arg Met Ser Val Ala Lys Thr Ser Val
945 950 955 960

Asp Ile Leu Lys Ile Leu Cys Asp Ile Gln Lys Asp Asn Leu Gln Lys
965 970 975

Lys Asp Glu Cys Glu Glu Met Leu Lys Leu Phe Lys Glu Val Ala Ser
980 985 990

Protein Complexes associated with APP-processing
 Leu Gln Glu Asn Phe Glu Val Phe Leu Ser Phe Glu Asp Tyr Ser Asn
 995 1000 1005

Ser Ser Leu Val Ala Asp Leu Arg Glu Gln His Ile Lys Ala His
 1010 1015 1020

Glu Val Ala Gln Ala Lys His Lys Pro Gly Ser Thr Pro Glu Pro
 1025 1030 1035

Ile Ala Ala Glu Val Arg Ser Pro Ser Met Glu Ser Lys Leu His
 1040 1045 1050

Arg Gln Ala Leu Ala Leu Gln Met Ser Lys Gln Glu Leu Glu Ala
 1055 1060 1065

Glu Leu Thr Leu Arg Ala Leu Lys Asp Gly Asn Ile Lys Thr Ala
 1070 1075 1080

Leu Lys Lys Cys Ser Asp Leu Phe Lys Tyr His Cys Asn Ala Asp
 1085 1090 1095

Thr Gly Lys Leu Leu Phe Leu Thr Cys Gln Lys Leu Cys Gln Met
 1100 1105 1110

Leu Ala Asp Asn Val Pro Val Thr Val Pro Val Gly Leu Asn Leu
 1115 1120 1125

Pro Ser Met Ile His Asp Leu Ala Ser Gln Ala Ala Thr Ile Cys
 1130 1135 1140

Ser Pro Asp Phe Leu Leu Asp Ala Leu Glu Leu Cys Lys His Thr
 1145 1150 1155

Leu Met Ala Val Glu Leu Ser Arg Gln Cys Gln Met Asp Asp Cys
 1160 1165 1170

Gly Ile Leu Met Lys Ala Ser Phe Gly Thr His Lys Asp Pro Tyr
 1175 1180 1185

Glu Glu Trp Ser Tyr Ser Asp Phe Phe Ser Glu Asp Gly Ile Val
 1190 1195 1200

Leu Glu Ser Gln Met Val Leu Pro Val Ile Tyr Glu Leu Ile Ser
 1205 1210 1215

Ser Leu Val Pro Leu Ala Glu Ser Lys Arg Tyr Pro Leu Glu Ser
 1220 1225 1230

Thr Ser Leu Pro Tyr Cys Ser Leu Asn Glu Gly Asp Gly Leu Val
 1235 1240 1245

Protein Complexes associated with APP-processing

Leu	Pro	Val	Ile	Asn	Ser	Ile	Ser	Ala	Leu	Leu	Gln	Asn	Leu	Gln
	1250					1255					1260			
Glu	Ser	Ser	Gln	Trp	Glu	Leu	Ala	Leu	Arg	Phe	Val	Val	Gly	Ser
	1265					1270					1275			
Phe	Gly	Thr	Cys	Leu	Gln	His	Ser	Val	Ser	Asn	Phe	Met	Asn	Ala
	1280					1285					1290			
Thr	Leu	Ser	Glu	Lys	Leu	Phe	Gly	Glu	Thr	Thr	Leu	Val	Lys	Ser
	1295					1300					1305			
Arg	His	Val	Val	Met	Glu	Leu	Lys	Glu	Lys	Ala	Val	Ile	Phe	Ile
	1310					1315					1320			
Arg	Glu	Asn	Ala	Thr	Thr	Leu	Leu	His	Lys	Val	Phe	Asn	Cys	Arg
	1325					1330					1335			
Leu	Val	Asp	Leu	Asp	Leu	Ala	Leu	Gly	Tyr	Cys	Thr	Leu	Leu	Pro
	1340					1345					1350			
Gln	Lys	Asp	Val	Phe	Glu	Asn	Leu	Trp	Lys	Leu	Ile	Asp	Lys	Ala
	1355					1360					1365			
Trp	Gln	Asn	Tyr	Asp	Lys	Ile	Leu	Ala	Ile	Ser	Leu	Val	Gly	Ser
	1370					1375					1380			
Glu	Leu	Ala	Ser	Leu	Tyr	Gln	Glu	Ile	Glu	Met	Gly	Leu	Lys	Phe
	1385					1390					1395			
Arg	Glu	Leu	Ser	Thr	Asp	Ala	Gln	Trp	Gly	Ile	Arg	Leu	Gly	Lys
	1400					1405					1410			
Leu	Gly	Ile	Ser	Phe	Gln	Pro	Val	Phe	Arg	Gln	His	Phe	Leu	Thr
	1415					1420					1425			
Lys	Lys	Asp	Leu	Ile	Lys	Ala	Leu	Val	Glu	Asn	Ile	Asp	Met	Asp
	1430					1435					1440			
Thr	Ser	Leu	Ile	Leu	Glu	Tyr	Cys	Ser	Thr	Phe	Gln	Leu	Asp	Cys
	1445					1450					1455			
Asp	Ala	Val	Leu	Gln	Leu	Phe	Ile	Glu	Thr	Leu	Leu	His	Asn	Thr
	1460					1465					1470			
Asn	Ala	Gly	Gln	Gly	Gln	Gly	Asp	Ala	Ser	Met	Asp	Ser	Ala	Lys
	1475					1480					1485			
Arg	Arg	His	Pro	Lys	Leu	Leu	Ala	Lys	Ala	Leu	Glu	Met	Val	Pro
	1490					1495					1500			

Protein Complexes associated with APP-processing

Leu Leu Thr Ser Thr Lys Asp Leu Val Ile Ser Leu Ser Gly Ile
1505 1510 1515

Leu His Lys Leu Asp Pro Tyr Asp Tyr Glu Met Ile Glu Val Val
1520 1525 1530

Leu Lys Val Ile Glu Arg Ala Asp Glu Lys Ile Thr Asn Ile Asn
1535 1540 1545

Ile Asn Gln Ala Leu Ser Ile Leu Lys His Leu Lys Ser Tyr Arg
1550 1555 1560

Arg Ile Ser Pro Pro Val Asp Leu Glu Tyr Gln Tyr Met Leu Glu
1565 1570 1575

His Val Ile Thr Leu Pro Ser Ala Ala Gln Thr Arg Leu Pro Phe
1580 1585 1590

His Leu Ile Phe Phe Gly Thr Ala Gln Asn Phe Trp Lys Ile Leu
1595 1600 1605

Ser Thr Glu Leu Ser Glu Glu Ser Phe Pro Thr Leu Leu Leu Ile
1610 1615 1620

Ser Lys Leu Met Lys Phe Ser Leu Asp Thr Leu Tyr Val Ser Thr
1625 1630 1635

Ala Lys His Val Phe Glu Lys Lys Leu Lys Pro Lys Leu Leu Lys
1640 1645 1650

Leu Thr Gln Ala Lys Ser Ser Thr Leu Ile Asn Lys Glu Ile Thr
1655 1660 1665

Lys Ile Thr Gln Thr Ile Glu Ser Cys Leu Leu Ser Ile Val Asn
1670 1675 1680

Pro Glu Trp Ala Val Ala Ile Ala Ile Ser Leu Ala Gln Asp Ile
1685 1690 1695

Pro Glu Gly Ser Phe Lys Ile Ser Ala Leu Lys Phe Cys Leu Tyr
1700 1705 1710

Leu Ala Glu Arg Trp Leu Gln Asn Ile Pro Ser Gln Asp Glu Lys
1715 1720 1725

Arg Glu Lys Ala Glu Ala Leu Leu Lys Lys Leu His Ile Gln Tyr
1730 1735 1740

Arg Arg Ser Gly Thr Glu Ala Val Leu Ile Ala His Lys Leu Asn
1745 1750 1755

Protein Complexes associated with APP-processing

Thr	Glu	Glu	Tyr	Leu	Arg	Val	Ile	Gly	Lys	Pro	Ala	His	Leu	Ile
	1760					1765					1770			
Val	Ser	Leu	Tyr	Glu	His	Pro	Ser	Ile	Asn	Gln	Arg	Ile	Gln	Asn
	1775					1780					1785			
Ser	Ser	Gly	Thr	Asp	Tyr	Pro	Asp	Ile	His	Ala	Ala	Ala	Lys	Glu
	1790					1795					1800			
Ile	Ala	Glu	Val	Asn	Glu	Ile	Asn	Leu	Glu	Lys	Val	Trp	Asp	Met
	1805					1810					1815			
Leu	Leu	Glu	Lys	Trp	Leu	Cys	Pro	Ser	Thr	Lys	Pro	Gly	Glu	Lys
	1820					1825					1830			
Pro	Ser	Glu	Leu	Phe	Glu	Leu	Gln	Glu	Asp	Glu	Ala	Leu	Arg	Arg
	1835					1840					1845			
Val	Gln	Tyr	Leu	Leu	Leu	Ser	Arg	Pro	Ile	Asp	Tyr	Ser	Ser	Arg
	1850					1855					1860			
Met	Leu	Phe	Val	Phe	Ala	Thr	Ser	Thr	Thr	Thr	Thr	Leu	Gly	Met
	1865					1870					1875			
His	Gln	Leu	Thr	Phe	Ala	His	Arg	Thr	Arg	Ala	Leu	Gln	Cys	Leu
	1880					1885					1890			
Phe	Tyr	Leu	Ala	Asp	Lys	Glu	Thr	Ile	Glu	Ser	Leu	Phe	Lys	Lys
	1895					1900					1905			
Pro	Ile	Glu	Glu	Val	Lys	Ser	Tyr	Leu	Arg	Cys	Ile	Thr	Phe	Leu
	1910					1915					1920			
Ala	Ser	Phe	Glu	Thr	Leu	Asn	Ile	Pro	Ile	Thr	Tyr	Glu	Leu	Phe
	1925					1930					1935			
Cys	Ser	Ser	Pro	Lys	Glu	Gly	Met	Ile	Lys	Gly	Leu	Trp	Lys	Asn
	1940					1945					1950			
His	Ser	His	Glu	Ser	Met	Ala	Val	Arg	Leu	Val	Thr	Glu	Leu	Cys
	1955					1960					1965			
Leu	Glu	Tyr	Lys	Ile	Tyr	Asp	Leu	Gln	Leu	Trp	Asn	Gly	Leu	Leu
	1970					1975					1980			
Gln	Lys	Leu	Leu	Gly	Phe	Asn	Met	Ile	Pro	Tyr	Leu	Arg	Lys	Val
	1985					1990					1995			
Leu	Lys	Ala	Ile	Ser	Ser	Ile	His	Ser	Leu	Trp	Gln	Val	Pro	Tyr
	2000					2005					2010			

Protein Complexes associated with APP-processing

Phe	Ser	Lys	Ala	Trp	Gln	Arg	Val	Ile	Gln	Ile	Pro	Leu	Leu	Ser
2015						2020					2025			
Ala	Ser	Cys	Pro	Leu	Ser	Pro	Asp	Gln	Leu	Ser	Asp	Cys	Ser	Glu
2030						2035					2040			
Ser	Leu	Ile	Ala	Val	Leu	Glu	Cys	Pro	Val	Ser	Gly	Asp	Leu	Asp
2045						2050					2055			
Leu	Ile	Gly	Val	Ala	Arg	Gln	Tyr	Ile	Gln	Leu	Glu	Leu	Pro	Ala
2060						2065					2070			
Phe	Ala	Leu	Ala	Cys	Leu	Met	Leu	Met	Pro	His	Ser	Glu	Lys	Arg
2075						2080					2085			
His	Gln	Gln	Ile	Lys	Asn	Phe	Leu	Gly	Ser	Cys	Asp	Pro	Gln	Val
2090						2095					2100			
Ile	Leu	Lys	Gln	Leu	Glu	Glu	His	Met	Asn	Thr	Gly	Gln	Leu	Ala
2105						2110					2115			
Gly	Phe	Ser	His	Gln	Ile	Arg	Ser	Leu	Ile	Leu	Asn	Asn	Ile	Ile
2120						2125					2130			
Asn	Lys	Lys	Glu	Phe	Gly	Ile	Leu	Ala	Lys	Thr	Lys	Tyr	Phe	Gln
2135						2140					2145			
Met	Leu	Lys	Met	His	Ala	Met	Asn	Thr	Asn	Asn	Ile	Thr	Glu	Leu
2150						2155					2160			
Val	Asn	Tyr	Leu	Ala	Asn	Asp	Leu	Ser	Leu	Asp	Glu	Ala	Ser	Val
2165						2170					2175			
Leu	Ile	Thr	Glu	Tyr	Ser	Lys	His	Cys	Gly	Lys	Pro	Val	Pro	Pro
2180						2185					2190			
Asp	Thr	Ala	Pro	Cys	Glu	Ile	Leu	Lys	Met	Phe	Leu	Ser	Gly	Leu
2195						2200					2205			

Ser

<210> 68

<211> 4647

<212> PRT

<213> Homo sapiens

<400> 68

Protein Complexes associated with APP-processing

Met Ser Glu Pro Gly Gly Gly Gly Gly Glu Asp Gly Ser Ala Gly Leu
1 5 10 15

Glu Val Ser Ala Val Gln Asn Val Ala Asp Val Ser Val Leu Gln Lys
20 25 30

His Leu Arg Lys Leu Val Pro Leu Leu Leu Glu Asp Gly Gly Glu Ala
35 40 45

Pro Ala Ala Leu Glu Ala Ala Leu Glu Glu Lys Ser Ala Leu Glu Gln
50 55 60

Met Arg Lys Phe Leu Ser Asp Pro Gln Val His Thr Val Leu Val Glu
65 70 75 80

Arg Ser Thr Leu Lys Glu Asp Val Gly Asp Glu Gly Glu Glu Glu Lys
85 90 95

Glu Phe Ile Ser Tyr Asn Ile Asn Ile Asp Ile His Tyr Gly Val Lys
100 105 110

Ser Asn Ser Leu Ala Phe Ile Lys Arg Thr Pro Val Ile Asp Ala Asp
115 120 125

Lys Pro Val Ser Ser Gln Leu Arg Val Leu Thr Leu Ser Glu Asp Ser
130 135 140

Pro Tyr Glu Thr Leu His Ser Phe Ile Ser Asn Ala Val Ala Pro Phe
145 150 155 160

Phe Lys Ser Tyr Ile Arg Glu Ser Gly Lys Ala Asp Arg Asp Gly Asp
165 170 175

Lys Met Ala Pro Ser Val Glu Lys Lys Ile Ala Glu Leu Glu Met Gly
180 185 190

Leu Leu His Leu Gln Gln Asn Ile Glu Ile Pro Glu Ile Ser Leu Pro
195 200 205

Ile His Pro Met Ile Thr Asn Val Ala Lys Gln Cys Tyr Glu Arg Gly
210 215 220

Glu Lys Pro Lys Val Thr Asp Phe Gly Asp Lys Val Glu Asp Pro Thr
225 230 235 240

Phe Leu Asn Gln Leu Gln Ser Gly Val Asn Arg Trp Ile Arg Glu Ile
245 250 255

Gln Lys Val Thr Lys Leu Asp Arg Asp Pro Ala Ser Gly Thr Ala Leu
260 265 270

Protein Complexes associated with APP-processing

Gln Glu Ile Ser Phe Trp Leu Asn Leu Glu Arg Ala Leu Tyr Arg Ile
 275 280 285

Gln Glu Lys Arg Glu Ser Pro Glu Val Leu Leu Thr Leu Asp Ile Leu
 290 295 300

Lys His Gly Lys Arg Phe His Ala Thr Val Ser Phe Asp Thr Asp Thr
 305 310 315 320

Gly Leu Lys Gln Ala Leu Glu Thr Val Asn Asp Tyr Asn Pro Leu Met
 325 330 335

Lys Asp Phe Pro Leu Asn Asp Leu Leu Ser Ala Thr Glu Leu Asp Lys
 340 345 350

Ile Arg Gln Ala Leu Val Ala Ile Phe Thr His Leu Arg Lys Ile Arg
 355 360 365

Asn Thr Lys Tyr Pro Ile Gln Arg Ala Leu Arg Leu Val Glu Ala Ile
 370 375 380

Ser Arg Asp Leu Ser Ser Gln Leu Leu Lys Val Leu Gly Thr Arg Lys
 385 390 395 400

Leu Met His Val Ala Tyr Glu Glu Phe Glu Lys Val Met Val Ala Cys
 405 410 415

Phe Glu Val Phe Gln Thr Trp Asp Asp Glu Tyr Glu Lys Leu Gln Val
 420 425 430

Leu Leu Arg Asp Ile Val Lys Arg Lys Arg Glu Glu Asn Leu Lys Met
 435 440 445

Val Trp Arg Ile Asn Pro Ala His Arg Lys Leu Gln Ala Arg Leu Asp
 450 455 460

Gln Met Arg Lys Phe Arg Arg Gln His Glu Gln Leu Arg Ala Val Ile
 465 470 475 480

Val Arg Val Leu Arg Pro Gln Val Thr Ala Val Ala Gln Gln Asn Gln
 485 490 495

Gly Glu Val Pro Glu Pro Gln Asp Met Lys Val Ala Glu Val Leu Phe
 500 505 510

Asp Ala Ala Asp Ala Asn Ala Ile Glu Glu Val Asn Leu Ala Tyr Glu
 515 520 525

Asn Val Lys Glu Val Asp Gly Leu Asp Val Ser Lys Glu Gly Thr Glu
 530 535 540

Protein Complexes associated with APP-processing

Ala Trp Glu Ala Ala Met Lys Arg Tyr Asp Glu Arg Ile Asp Arg Val
545 550 555 560

Glu Thr Arg Ile Thr Ala Arg Leu Arg Asp Gln Leu Gly Thr Ala Lys
565 570 575

Asn Ala Asn Glu Met Phe Arg Ile Phe Ser Arg Phe Asn Ala Leu Phe
580 585 590

Val Arg Pro His Ile Arg Gly Ala Ile Arg Glu Tyr Gln Thr Gln Leu
595 600 605

Ile Gln Arg Val Lys Asp Asp Ile Glu Ser Leu His Asp Lys Phe Lys
610 615 620

Val Gln Tyr Pro Gln Ser Gln Ala Cys Lys Met Ser His Val Arg Asp
625 630 635 640

Leu Pro Pro Val Ser Gly Ser Ile Ile Trp Ala Lys Gln Ile Asp Arg
645 650 655

Gln Leu Thr Ala Tyr Met Lys Arg Val Glu Asp Val Leu Gly Lys Gly
660 665 670

Trp Glu Asn His Val Glu Gly Gln Lys Leu Lys Gln Asp Gly Asp Ser
675 680 685

Phe Arg Met Lys Leu Asn Thr Gln Glu Ile Phe Asp Asp Trp Ala Arg
690 695 700

Lys Val Gln Gln Arg Asn Leu Gly Val Ser Gly Arg Ile Phe Thr Ile
705 710 715 720

Glu Ser Thr Arg Val Arg Gly Arg Thr Gly Asn Val Leu Lys Leu Lys
725 730 735

Val Asn Phe Leu Pro Glu Ile Ile Thr Leu Ser Lys Glu Val Arg Asn
740 745 750

Leu Lys Trp Leu Gly Phe Arg Val Pro Leu Ala Ile Val Asn Lys Ala
755 760 765

His Gln Ala Asn Gln Leu Tyr Pro Phe Ala Ile Ser Leu Ile Glu Ser
770 775 780

Val Arg Thr Tyr Glu Arg Thr Cys Glu Lys Val Glu Glu Arg Asn Thr
785 790 795 800

Ile Ser Leu Leu Val Ala Gly Leu Lys Lys Glu Val Gln Ala Leu Ile
805 810 815

Protein Complexes associated with APP-processing

Ala Glu Gly Ile Ala Leu Val Trp Glu Ser Tyr Lys Leu Asp Pro Tyr
 820 825 830

Val Gln Arg Leu Ala Glu Thr Val Phe Asn Phe Gln Glu Lys Val Asp
 835 840 845

Asp Leu Leu Ile Ile Glu Glu Lys Ile Asp Leu Glu Val Arg Ser Leu
 850 855 860

Glu Thr Cys Met Tyr Asp His Lys Thr Phe Ser Glu Ile Leu Asn Arg
 865 870 875 880

Val Gln Lys Ala Val Asp Asp Leu Asn Leu His Ser Tyr Ser Asn Leu
 885 890 895

Pro Ile Trp Val Asn Lys Leu Asp Met Glu Ile Glu Arg Ile Leu Gly
 900 905 910

Val Arg Leu Gln Ala Gly Leu Arg Ala Trp Thr Gln Val Leu Leu Gly
 915 920 925

Gln Ala Glu Asp Lys Ala Glu Val Asp Met Asp Thr Asp Ala Pro Gln
 930 935 940

Val Ser His Lys Pro Gly Gly Glu Pro Lys Ile Lys Asn Val Val His
 945 950 955 960

Glu Leu Arg Ile Thr Asn Gln Val Ile Tyr Leu Asn Pro Pro Ile Glu
 965 970 975

Glu Cys Arg Tyr Lys Leu Tyr Gln Glu Met Phe Ala Trp Lys Met Val
 980 985 990

Val Leu Ser Leu Pro Arg Ile Gln Ser Gln Arg Tyr Gln Val Gly Val
 995 1000 1005

His Tyr Glu Leu Thr Glu Glu Glu Lys Phe Tyr Arg Asn Ala Leu
 1010 1015 1020

Thr Arg Met Pro Asp Gly Pro Val Ala Leu Glu Glu Ser Tyr Ser
 1025 1030 1035

Ala Val Met Gly Ile Val Ser Glu Val Glu Gln Tyr Val Lys Val
 1040 1045 1050

Trp Leu Gln Tyr Gln Cys Leu Trp Asp Met Gln Ala Glu Asn Ile
 1055 1060 1065

Tyr Asn Arg Leu Gly Glu Asp Leu Asn Lys Trp Gln Ala Leu Leu
 1070 1075 1080

Protein Complexes associated with APP-processing

Val	Gln	Ile	Arg	Lys	Ala	Arg	Gly	Thr	Phe	Asp	Asn	Ala	Glu	Thr
	1085					1090					1095			
Lys	Lys	Glu	Phe	Gly	Pro	Val	Val	Ile	Asp	Tyr	Gly	Lys	Val	Gln
	1100					1105					1110			
Ser	Lys	Val	Asn	Leu	Lys	Tyr	Asp	Ser	Trp	His	Lys	Glu	Val	Leu
	1115					1120					1125			
Ser	Lys	Phe	Gly	Gln	Met	Leu	Gly	Ser	Asn	Met	Thr	Glu	Phe	His
	1130					1135					1140			
Ser	Gln	Ile	Ser	Lys	Ser	Arg	Gln	Glu	Leu	Glu	Gln	His	Ser	Val
	1145					1150					1155			
Asp	Thr	Ala	Ser	Thr	Ser	Asp	Ala	Val	Thr	Phe	Ile	Thr	Tyr	Val
	1160					1165					1170			
Gln	Ser	Leu	Lys	Arg	Lys	Ile	Lys	Gln	Phe	Glu	Lys	Gln	Val	Glu
	1175					1180					1185			
Leu	Tyr	Arg	Asn	Gly	Gln	Arg	Leu	Leu	Glu	Lys	Gln	Arg	Phe	Gln
	1190					1195					1200			
Phe	Pro	Pro	Ser	Trp	Leu	Tyr	Ile	Asp	Asn	Ile	Glu	Gly	Glu	Trp
	1205					1210					1215			
Gly	Ala	Phe	Asn	Asp	Ile	Met	Arg	Arg	Lys	Asp	Ser	Ala	Ile	Gln
	1220					1225					1230			
Gln	Gln	Val	Ala	Asn	Leu	Gln	Met	Lys	Ile	Val	Gln	Glu	Asp	Arg
	1235					1240					1245			
Ala	Val	Glu	Ser	Arg	Thr	Thr	Asp	Leu	Leu	Thr	Asp	Trp	Glu	Lys
	1250					1255					1260			
Thr	Lys	Pro	Val	Thr	Gly	Asn	Leu	Arg	Pro	Glu	Glu	Ala	Leu	Gln
	1265					1270					1275			
Ala	Leu	Thr	Ile	Tyr	Glu	Gly	Lys	Phe	Gly	Arg	Leu	Lys	Asp	Asp
	1280					1285					1290			
Arg	Glu	Lys	Cys	Ala	Lys	Ala	Lys	Glu	Ala	Leu	Glu	Leu	Thr	Asp
	1295					1300					1305			
Thr	Gly	Leu	Leu	Ser	Gly	Ser	Glu	Glu	Arg	Val	Gln	Val	Ala	Leu
	1310					1315					1320			
Glu	Glu	Leu	Gln	Asp	Leu	Lys	Gly	Val	Trp	Ser	Glu	Leu	Ser	Lys
	1325					1330					1335			

Protein Complexes associated with APP-processing

Val Trp Glu Gln Ile Asp Gln Met Lys Glu Gln Pro Trp Val Ser
 1340 1345 1350

Val Gln Pro Arg Lys Leu Arg Gln Asn Leu Asp Ala Leu Leu Asn
 1355 1360 1365

Gln Leu Lys Ser Phe Pro Ala Arg Leu Arg Gln Tyr Ala Ser Tyr
 1370 1375 1380

Glu Phe Val Gln Arg Leu Leu Lys Gly Tyr Met Lys Ile Asn Met
 1385 1390 1395

Leu Val Ile Glu Leu Lys Ser Glu Ala Leu Lys Asp Arg His Trp
 1400 1405 1410

Lys Gln Leu Met Lys Arg Leu His Val Asn Trp Val Val Ser Glu
 1415 1420 1425

Leu Thr Leu Gly Gln Ile Trp Asp Val Asp Leu Gln Lys Asn Glu
 1430 1435 1440

Ala Ile Val Lys Asp Val Leu Leu Val Ala Gln Gly Glu Met Ala
 1445 1450 1455

Leu Glu Glu Phe Leu Lys Gln Ala Lys Val Trp Asn Thr Tyr Glu
 1460 1465 1470

Leu Asp Leu Val Asn Tyr Gln Asn Lys Cys Arg Leu Ile Arg Gly
 1475 1480 1485

Trp Asp Asp Leu Phe Asn Lys Val Lys Glu His Ile Asn Ser Val
 1490 1495 1500

Ser Ala Met Lys Leu Ser Pro Tyr Tyr Lys Val Phe Glu Glu Asp
 1505 1510 1515

Ala Leu Ser Trp Glu Asp Lys Leu Asn Arg Ile Met Ala Leu Phe
 1520 1525 1530

Asp Val Trp Ile Asp Val Gln Arg Arg Trp Val Tyr Leu Glu Gly
 1535 1540 1545

Ile Phe Thr Gly Ser Ala Asp Ile Lys His Leu Leu Pro Val Glu
 1550 1555 1560

Thr Gln Arg Phe Gln Ser Ile Ser Thr Glu Phe Leu Ala Leu Met
 1565 1570 1575

Lys Lys Val Ser Lys Ser Pro Leu Val Met Asp Val Leu Asn Ile
 1580 1585 1590

Protein Complexes associated with APP-processing

Gln	Gly	Val	Gln	Arg	Ser	Leu	Glu	Arg	Leu	Ala	Asp	Leu	Leu	Gly
	1595					1600					1605			
Lys	Ile	Gln	Lys	Ala	Leu	Gly	Glu	Tyr	Leu	Glu	Arg	Glu	Arg	Ser
	1610					1615					1620			
Ser	Phe	Pro	Arg	Phe	Tyr	Phe	Val	Gly	Asp	Glu	Asp	Leu	Leu	Glu
	1625					1630					1635			
Ile	Ile	Gly	Asn	Ser	Lys	Asn	Val	Ala	Lys	Leu	Gln	Lys	His	Phe
	1640					1645					1650			
Lys	Lys	Met	Phe	Ala	Gly	Val	Ser	Ser	Ile	Ile	Leu	Asn	Glu	Asp
	1655					1660					1665			
Asn	Ser	Val	Val	Leu	Gly	Ile	Ser	Ser	Arg	Glu	Gly	Glu	Glu	Val
	1670					1675					1680			
Met	Phe	Lys	Thr	Pro	Val	Ser	Ile	Thr	Glu	His	Pro	Lys	Ile	Asn
	1685					1690					1695			
Glu	Trp	Leu	Thr	Leu	Val	Glu	Lys	Glu	Met	Arg	Val	Thr	Leu	Ala
	1700					1705					1710			
Lys	Leu	Leu	Ala	Glu	Ser	Val	Thr	Glu	Val	Glu	Ile	Phe	Gly	Lys
	1715					1720					1725			
Ala	Thr	Ser	Ile	Asp	Pro	Asn	Thr	Tyr	Ile	Thr	Trp	Ile	Asp	Lys
	1730					1735					1740			
Tyr	Gln	Ala	Gln	Leu	Val	Val	Leu	Ser	Ala	Gln	Ile	Ala	Trp	Ser
	1745					1750					1755			
Glu	Asn	Val	Glu	Thr	Ala	Leu	Ser	Ser	Met	Gly	Gly	Gly	Gly	Asp
	1760					1765					1770			
Ala	Ala	Pro	Leu	His	Ser	Val	Leu	Ser	Asn	Val	Glu	Val	Thr	Leu
	1775					1780					1785			
Asn	Val	Leu	Ala	Asp	Ser	Val	Leu	Met	Glu	Gln	Pro	Pro	Leu	Arg
	1790					1795					1800			
Arg	Arg	Lys	Leu	Glu	His	Leu	Ile	Thr	Glu	Leu	Val	His	Gln	Arg
	1805					1810					1815			
Asp	Val	Thr	Arg	Ser	Leu	Ile	Lys	Ser	Lys	Ile	Asp	Asn	Ala	Lys
	1820					1825					1830			
Ser	Phe	Glu	Trp	Leu	Ser	Gln	Met	Arg	Phe	Tyr	Phe	Asp	Pro	Lys
	1835					1840					1845			

Protein Complexes associated with APP-processing

Gln Thr Asp Val Leu Gln Gln Leu Ser Ile Gln Met Ala Asn Ala
 1850 1855 1860

Lys Phe Asn Tyr Gly Phe Glu Tyr Leu Gly Val Gln Asp Lys Leu
 1865 1870 1875

Val Gln Thr Pro Leu Thr Asp Arg Cys Tyr Leu Thr Met Thr Gln
 1880 1885 1890

Ala Leu Glu Ala Arg Leu Gly Gly Ser Pro Phe Gly Pro Ala Gly
 1895 1900 1905

Thr Gly Lys Thr Glu Ser Val Lys Ala Leu Gly His Gln Leu Gly
 1910 1915 1920

Arg Phe Val Leu Val Phe Asn Cys Asp Glu Thr Phe Asp Phe Gln
 1925 1930 1935

Ala Met Gly Arg Ile Phe Val Gly Leu Cys Gln Val Gly Ala Trp
 1940 1945 1950

Gly Cys Phe Asp Glu Phe Asn Arg Leu Glu Glu Arg Met Leu Ser
 1955 1960 1965

Ala Val Ser Gln Gln Val Gln Cys Ile Gln Glu Ala Leu Arg Glu
 1970 1975 1980

His Ser Asn Pro Asn Tyr Asp Lys Thr Ser Ala Pro Ile Thr Cys
 1985 1990 1995

Glu Leu Leu Asn Lys Gln Val Lys Val Ser Pro Asp Met Ala Ile
 2000 2005 2010

Phe Ile Thr Met Asn Pro Gly Tyr Ala Gly Arg Ser Asn Leu Pro
 2015 2020 2025

Asp Asn Leu Lys Lys Leu Phe Arg Ser Leu Ala Met Thr Lys Pro
 2030 2035 2040

Asp Arg Gln Leu Ile Ala Gln Val Met Leu Tyr Ser Gln Gly Phe
 2045 2050 2055

Arg Thr Ala Glu Val Leu Ala Asn Lys Ile Val Pro Phe Phe Lys
 2060 2065 2070

Leu Cys Asp Glu Gln Leu Ser Ser Gln Ser His Tyr Asp Phe Gly
 2075 2080 2085

Leu Arg Ala Leu Lys Ser Val Leu Val Ser Ala Gly Asn Val Lys
 2090 2095 2100

Protein Complexes associated with APP-processing

Arg Glu Arg Ile Gln Lys Ile Lys Arg Glu Lys Glu Glu Arg Gly
 2105 2110 2115

Glu Ala Val Asp Glu Gly Glu Ile Ala Glu Asn Leu Pro Glu Gln
 2120 2125 2130

Glu Ile Leu Ile Gln Ser Val Cys Glu Thr Met Val Pro Lys Leu
 2135 2140 2145

Val Ala Glu Asp Ile Pro Leu Leu Phe Ser Leu Leu Ser Asp Val
 2150 2155 2160

Phe Pro Gly Val Gln Tyr His Arg Gly Glu Met Thr Ala Leu Arg
 2165 2170 2175

Glu Glu Leu Lys Lys Val Cys Gln Glu Met Tyr Leu Thr Tyr Gly
 2180 2185 2190

Asp Gly Glu Glu Val Gly Gly Met Trp Val Glu Lys Val Leu Gln
 2195 2200 2205

Leu Tyr Gln Ile Thr Gln Ile Asn His Gly Leu Met Met Val Gly
 2210 2215 2220

Pro Ser Gly Ser Gly Lys Ser Met Ala Trp Arg Val Leu Leu Lys
 2225 2230 2235

Ala Leu Glu Arg Leu Glu Gly Val Glu Gly Val Ala His Ile Ile
 2240 2245 2250

Asp Pro Lys Ala Ile Ser Lys Asp His Leu Tyr Gly Thr Leu Asp
 2255 2260 2265

Pro Asn Thr Arg Glu Trp Thr Asp Gly Leu Phe Thr His Val Leu
 2270 2275 2280

Arg Lys Ile Ile Asp Ser Val Arg Gly Glu Leu Gln Lys Arg Gln
 2285 2290 2295

Trp Ile Val Phe Asp Gly Asp Val Asp Pro Glu Trp Val Glu Asn
 2300 2305 2310

Leu Asn Ser Val Leu Asp Asp Asn Lys Leu Leu Thr Leu Pro Asn
 2315 2320 2325

Gly Glu Arg Leu Ser Leu Pro Pro Asn Val Arg Ile Met Phe Glu
 2330 2335 2340

Val Gln Asp Leu Lys Tyr Ala Thr Leu Ala Thr Val Ser Arg Cys
 2345 2350 2355

Protein Complexes associated with APP-processing

Gly	Met	Val	Trp	Phe	Ser	Glu	Asp	Val	Leu	Ser	Thr	Asp	Met	Ile
	2360					2365					2370			
Phe	Asn	Asn	Phe	Leu	Ala	Arg	Leu	Arg	Ser	Ile	Pro	Leu	Asp	Glu
	2375					2380					2385			
Gly	Glu	Asp	Glu	Ala	Gln	Arg	Arg	Arg	Lys	Gly	Lys	Glu	Asp	Glu
	2390					2395					2400			
Gly	Glu	Glu	Ala	Ala	Ser	Pro	Met	Leu	Gln	Ile	Gln	Arg	Asp	Ala
	2405					2410					2415			
Ala	Thr	Ile	Met	Gln	Pro	Tyr	Phe	Thr	Ser	Asn	Gly	Leu	Val	Thr
	2420					2425					2430			
Lys	Ala	Leu	Glu	His	Ala	Phe	Gln	Leu	Glu	His	Ile	Met	Asp	Leu
	2435					2440					2445			
Thr	Arg	Leu	Arg	Cys	Leu	Gly	Ser	Leu	Phe	Ser	Met	Leu	His	Gln
	2450					2455					2460			
Ala	Cys	Arg	Asn	Val	Ala	Gln	Tyr	Asn	Ala	Asn	His	Pro	Asp	Phe
	2465					2470					2475			
Pro	Met	Gln	Ile	Glu	Gln	Leu	Glu	Arg	Tyr	Ile	Gln	Arg	Tyr	Leu
	2480					2485					2490			
Val	Tyr	Ala	Ile	Leu	Trp	Ser	Leu	Ser	Gly	Asp	Ser	Arg	Leu	Lys
	2495					2500					2505			
Met	Arg	Ala	Glu	Leu	Gly	Glu	Tyr	Ile	Arg	Arg	Ile	Thr	Thr	Val
	2510					2515					2520			
Pro	Leu	Pro	Thr	Ala	Pro	Asn	Ile	Pro	Ile	Ile	Asp	Tyr	Glu	Val
	2525					2530					2535			
Ser	Ile	Ser	Gly	Glu	Trp	Ser	Pro	Trp	Gln	Ala	Lys	Val	Pro	Gln
	2540					2545					2550			
Ile	Glu	Val	Glu	Thr	His	Lys	Val	Ala	Ala	Pro	Asp	Val	Val	Val
	2555					2560					2565			
Pro	Thr	Leu	Asp	Thr	Val	Arg	His	Glu	Ala	Leu	Leu	Tyr	Thr	Trp
	2570					2575					2580			
Leu	Ala	Glu	His	Lys	Pro	Leu	Val	Leu	Cys	Gly	Pro	Pro	Gly	Ser
	2585					2590					2595			
Gly	Lys	Thr	Met	Thr	Leu	Phe	Ser	Ala	Leu	Arg	Ala	Leu	Pro	Asp
	2600					2605					2610			

Protein Complexes associated with APP-processing

Met Glu Val Val Gly Leu Asn Phe Ser Ser Ala Thr Thr Pro Glu
 2615 2620 2625

Leu Leu Leu Lys Thr Phe Asp His Tyr Cys Glu Tyr Arg Arg Thr
 2630 2635 2640

Pro Asn Gly Val Val Leu Ala Pro Val Gln Leu Gly Lys Trp Leu
 2645 2650 2655

Val Leu Phe Cys Asp Glu Ile Asn Leu Pro Asp Met Asp Lys Tyr
 2660 2665 2670

Gly Thr Gln Arg Val Ile Ser Phe Ile Arg Gln Met Val Glu His
 2675 2680 2685

Gly Gly Phe Tyr Arg Thr Ser Asp Gln Thr Trp Val Lys Leu Glu
 2690 2695 2700

Arg Ile Gln Phe Val Gly Ala Cys Asn Pro Pro Thr Asp Pro Gly
 2705 2710 2715

Arg Lys Pro Leu Ser His Arg Phe Leu Arg His Val Pro Val Val
 2720 2725 2730

Tyr Val Asp Tyr Pro Gly Pro Ala Ser Leu Thr Gln Ile Tyr Gly
 2735 2740 2745

Thr Phe Asn Arg Ala Met Leu Arg Leu Ile Pro Ser Leu Arg Thr
 2750 2755 2760

Tyr Ala Glu Pro Leu Thr Ala Ala Met Val Glu Phe Tyr Thr Met
 2765 2770 2775

Ser Gln Glu Arg Phe Thr Gln Asp Thr Gln Pro His Tyr Ile Tyr
 2780 2785 2790

Ser Pro Arg Glu Met Thr Arg Trp Val Arg Gly Ile Phe Glu Ala
 2795 2800 2805

Leu Arg Pro Leu Glu Thr Leu Pro Val Glu Gly Leu Ile Arg Ile
 2810 2815 2820

Trp Ala His Glu Ala Leu Arg Leu Phe Gln Asp Arg Leu Val Glu
 2825 2830 2835

Asp Glu Glu Arg Arg Trp Thr Asp Glu Asn Ile Asp Thr Val Ala
 2840 2845 2850

Leu Lys His Phe Pro Asn Ile Asp Arg Glu Lys Ala Met Ser Arg
 2855 2860 2865

Protein Complexes associated with APP-processing

Pro Ile Leu Tyr Ser Asn Trp Leu Ser Lys Asp Tyr Ile Pro Val
 2870 2875 2880

Asp Gln Glu Glu Leu Arg Asp Tyr Val Lys Ala Arg Leu Lys Val
 2885 2890 2895

Phe Tyr Glu Glu Glu Leu Asp Val Pro Leu Val Leu Phe Asn Glu
 2900 2905 2910

Val Leu Asp His Val Leu Arg Ile Asp Arg Ile Phe Arg Gln Pro
 2915 2920 2925

Gln Gly His Leu Leu Leu Ile Gly Val Ser Gly Ala Gly Lys Thr
 2930 2935 2940

Thr Leu Ser Arg Phe Val Ala Trp Met Asn Gly Leu Ser Val Tyr
 2945 2950 2955

Gln Ile Lys Val His Arg Lys Tyr Thr Gly Glu Asp Phe Asp Glu
 2960 2965 2970

Asp Leu Arg Thr Val Leu Arg Arg Ser Gly Cys Lys Asn Glu Lys
 2975 2980 2985

Ile Ala Phe Ile Met Asp Glu Ser Asn Val Leu Asp Ser Gly Phe
 2990 2995 3000

Leu Glu Arg Met Asn Thr Leu Leu Ala Asn Gly Glu Val Pro Gly
 3005 3010 3015

Leu Phe Glu Gly Asp Glu Tyr Ala Thr Leu Met Thr Gln Cys Lys
 3020 3025 3030

Glu Gly Ala Gln Lys Glu Gly Leu Met Leu Asp Ser His Glu Glu
 3035 3040 3045

Leu Tyr Lys Trp Phe Thr Ser Gln Val Ile Arg Asn Leu His Val
 3050 3055 3060

Val Phe Thr Met Asn Pro Ser Ser Glu Gly Leu Lys Asp Arg Ala
 3065 3070 3075

Ala Thr Ser Pro Ala Leu Phe Asn Arg Cys Val Leu Asn Trp Phe
 3080 3085 3090

Gly Asp Trp Ser Thr Glu Ala Leu Tyr Gln Val Gly Lys Glu Phe
 3095 3100 3105

Thr Ser Lys Met Asp Leu Glu Lys Pro Asn Tyr Ile Val Pro Asp
 3110 3115 3120

Protein Complexes associated with APP-processing

Tyr Met Pro Val Val Tyr Asp Lys Leu Pro Gln Pro Pro Ser His
 3125 3130 3135

Arg Glu Ala Ile Val Asn Ser Cys Val Phe Val His Gln Thr Leu
 3140 3145 3150

His Gln Ala Asn Ala Arg Leu Ala Lys Arg Gly Gly Arg Thr Met
 3155 3160 3165

Ala Ile Thr Pro Arg His Tyr Leu Asp Phe Ile Asn His Tyr Ala
 3170 3175 3180

Asn Leu Phe His Glu Lys Arg Ser Glu Leu Glu Glu Gln Gln Met
 3185 3190 3195

His Leu Asn Val Gly Leu Arg Lys Ile Lys Glu Thr Val Asp Gln
 3200 3205 3210

Val Glu Glu Leu Arg Arg Asp Leu Arg Ile Lys Ser Gln Glu Leu
 3215 3220 3225

Glu Val Lys Asn Ala Ala Ala Asn Asp Lys Leu Lys Lys Met Val
 3230 3235 3240

Lys Asp Gln Gln Glu Ala Glu Lys Lys Lys Val Met Ser Gln Glu
 3245 3250 3255

Ile Gln Glu Gln Leu His Lys Gln Gln Glu Val Ile Ala Asp Lys
 3260 3265 3270

Gln Met Ser Val Lys Glu Asp Leu Asp Lys Val Glu Pro Ala Val
 3275 3280 3285

Ile Glu Ala Gln Asn Ala Val Lys Ser Ile Lys Lys Gln His Leu
 3290 3295 3300

Val Glu Val Arg Ser Met Ala Asn Pro Pro Ala Ala Val Lys Leu
 3305 3310 3315

Ala Leu Glu Ser Ile Cys Leu Leu Leu Gly Glu Ser Thr Thr Asp
 3320 3325 3330

Trp Lys Gln Ile Arg Ser Ile Ile Met Arg Glu Asn Phe Ile Pro
 3335 3340 3345

Thr Ile Val Asn Phe Ser Ala Glu Glu Ile Ser Asp Ala Ile Arg
 3350 3355 3360

Glu Lys Met Lys Lys Asn Tyr Met Ser Asn Pro Ser Tyr Asn Tyr
 3365 3370 3375

Protein Complexes associated with APP-processing

Glu Ile Val Asn Arg Ala Ser Leu Ala Cys Gly Pro Met Val Lys
 3380 3385 3390

Trp Ala Ile Ala Gln Leu Asn Tyr Ala Asp Met Leu Lys Arg Val
 3395 3400 3405

Glu Pro Leu Arg Asn Glu Leu Gln Lys Leu Glu Asp Asp Ala Lys
 3410 3415 3420

Asp Asn Gln Gln Lys Ala Asn Glu Val Glu Gln Met Ile Arg Asp
 3425 3430 3435

Leu Glu Ala Ser Ile Ala Arg Tyr Lys Glu Glu Tyr Ala Val Leu
 3440 3445 3450

Ile Ser Glu Ala Gln Ala Ile Lys Ala Asp Leu Ala Ala Val Glu
 3455 3460 3465

Ala Lys Val Asn Arg Ser Thr Ala Leu Leu Lys Ser Leu Ser Ala
 3470 3475 3480

Glu Arg Glu Arg Trp Glu Lys Thr Ser Glu Thr Phe Lys Asn Gln
 3485 3490 3495

Met Ser Thr Ile Ala Gly Asp Cys Leu Leu Ser Ala Ala Phe Ile
 3500 3505 3510

Ala Tyr Ala Gly Tyr Phe Asp Gln Gln Met Arg Gln Asn Leu Phe
 3515 3520 3525

Thr Thr Trp Ser His His Leu Gln Gln Ala Asn Ile Gln Phe Arg
 3530 3535 3540

Thr Asp Ile Ala Arg Thr Glu Tyr Leu Ser Asn Ala Asp Glu Arg
 3545 3550 3555

Leu Arg Trp Gln Ala Ser Ser Leu Pro Ala Asp Asp Leu Cys Thr
 3560 3565 3570

Glu Asn Ala Ile Met Leu Lys Arg Phe Asn Arg Tyr Pro Leu Ile
 3575 3580 3585

Ile Asp Pro Ser Gly Gln Ala Thr Glu Phe Ile Met Asn Glu Tyr
 3590 3595 3600

Lys Asp Arg Lys Ile Thr Arg Thr Ser Phe Leu Asp Asp Ala Phe
 3605 3610 3615

Arg Lys Asn Leu Glu Ser Ala Leu Arg Phe Gly Asn Pro Leu Leu
 3620 3625 3630

Protein Complexes associated with APP-processing

Val Gln Asp Val Glu Ser Tyr Asp Pro Val Leu Asn Pro Val Leu
3635 3640 3645

Asn Arg Glu Val Arg Arg Thr Gly Gly Arg Val Leu Ile Thr Leu
3650 3655 3660

Gly Asp Gln Asp Ile Asp Leu Ser Pro Ser Phe Val Ile Phe Leu
3665 3670 3675

Ser Thr Arg Asp Pro Thr Val Glu Phe Pro Pro Asp Leu Cys Ser
3680 3685 3690

Arg Val Thr Phe Val Asn Phe Thr Val Thr Arg Ser Ser Leu Gln
3695 3700 3705

Ser Gln Cys Leu Asn Glu Val Leu Lys Ala Glu Arg Pro Asp Val
3710 3715 3720

Asp Glu Lys Arg Ser Asp Leu Leu Lys Leu Gln Gly Glu Phe Gln
3725 3730 3735

Leu Arg Leu Arg Gln Leu Glu Lys Ser Leu Leu Gln Ala Leu Asn
3740 3745 3750

Glu Val Lys Gly Arg Ile Leu Asp Asp Asp Thr Ile Ile Thr Thr
3755 3760 3765

Leu Glu Asn Leu Lys Arg Glu Ala Ala Glu Val Thr Arg Lys Val
3770 3775 3780

Glu Glu Thr Asp Ile Val Met Gln Glu Val Glu Thr Val Ser Gln
3785 3790 3795

Gln Tyr Leu Pro Leu Ser Thr Ala Cys Ser Ser Ile Tyr Phe Thr
3800 3805 3810

Met Glu Ser Leu Lys Gln Ile His Phe Leu Tyr Gln Tyr Ser Leu
3815 3820 3825

Gln Phe Phe Leu Asp Ile Tyr His Asn Val Leu Tyr Glu Asn Pro
3830 3835 3840

Asn Leu Lys Gly Val Thr Asp His Thr Gln Arg Leu Ser Ile Ile
3845 3850 3855

Thr Lys Asp Leu Phe Gln Val Ala Phe Asn Arg Val Ala Arg Gly
3860 3865 3870

Met Leu His Gln Asp His Ile Thr Phe Ala Met Leu Leu Ala Arg
3875 3880 3885

Protein Complexes associated with APP-processing

Ile Lys Leu Lys Gly Thr Val Gly Glu Pro Thr Tyr Asp Ala Glu
 3890 3895 3900

Phe Gln His Phe Leu Arg Gly Asn Glu Ile Val Leu Ser Ala Gly
 3905 3910 3915

Ser Thr Pro Arg Ile Gln Gly Leu Thr Val Glu Gln Ala Glu Ala
 3920 3925 3930

Val Val Arg Leu Ser Cys Leu Pro Ala Phe Lys Asp Leu Ile Ala
 3935 3940 3945

Lys Val Gln Ala Asp Glu Gln Phe Gly Ile Trp Leu Asp Ser Ser
 3950 3955 3960

Ser Pro Glu Gln Thr Val Pro Tyr Leu Trp Ser Glu Glu Thr Pro
 3965 3970 3975

Ala Thr Pro Ile Gly Gln Ala Ile His Arg Leu Leu Leu Ile Gln
 3980 3985 3990

Ala Phe Arg Pro Asp Arg Leu Leu Ala Met Ala His Met Phe Val
 3995 4000 4005

Ser Thr Asn Leu Gly Glu Ser Phe Met Ser Ile Met Glu Gln Pro
 4010 4015 4020

Leu Asp Leu Thr His Ile Val Gly Thr Glu Val Lys Pro Asn Thr
 4025 4030 4035

Pro Val Leu Met Cys Ser Val Pro Gly Tyr Asp Ala Ser Gly His
 4040 4045 4050

Val Glu Asp Leu Ala Ala Glu Gln Asn Thr Gln Ile Thr Ser Ile
 4055 4060 4065

Ala Ile Gly Ser Ala Glu Gly Phe Asn Gln Ala Asp Lys Ala Ile
 4070 4075 4080

Asn Thr Ala Val Lys Ser Gly Arg Trp Val Met Leu Lys Asn Val
 4085 4090 4095

His Leu Ala Pro Gly Trp Leu Met Gln Leu Glu Lys Lys Leu His
 4100 4105 4110

Ser Leu Gln Pro His Ala Cys Phe Arg Leu Phe Leu Thr Met Glu
 4115 4120 4125

Ile Asn Pro Lys Val Pro Val Asn Leu Leu Arg Ala Gly Arg Ile
 4130 4135 4140

Protein Complexes associated with APP-processing

Phe Val Phe Glu Pro Pro Gly Val Lys Ala Asn Met Leu Arg
 4145 4150 4155

Thr Phe Ser Ser Ile Pro Val Ser Arg Ile Cys Lys Ser Pro Asn
 4160 4165 4170

Glu Arg Ala Arg Leu Tyr Phe Leu Leu Ala Trp Phe His Ala Ile
 4175 4180 4185

Ile Gln Glu Arg Leu Arg Tyr Ala Pro Leu Gly Trp Ser Lys Lys
 4190 4195 4200

Tyr Glu Phe Gly Glu Ser Asp Leu Arg Ser Ala Cys Asp Thr Val
 4205 4210 4215

Asp Thr Trp Leu Asp Asp Thr Ala Lys Ala Ser Gly Arg Gln Asn
 4220 4225 4230

Ile Ser Pro Asp Lys Ile Pro Trp Ser Ala Leu Lys Thr Leu Met
 4235 4240 4245

Ala Gln Ser Ile Tyr Gly Gly Arg Val Asp Asn Glu Phe Asp Gln
 4250 4255 4260

Arg Leu Leu Asn Thr Phe Leu Glu Arg Leu Phe Thr Thr Arg Ser
 4265 4270 4275

Phe Asp Ser Glu Phe Lys Leu Ala Cys Lys Val Asp Gly His Lys
 4280 4285 4290

Asp Ile Gln Met Pro Asp Gly Ile Arg Arg Glu Glu Phe Val Gln
 4295 4300 4305

Trp Val Glu Leu Leu Pro Asp Thr Gln Thr Pro Ser Trp Leu Gly
 4310 4315 4320

Leu Pro Asn Asn Ala Glu Arg Val Leu Leu Thr Thr Gln Gly Val
 4325 4330 4335

Asp Met Ile Ser Lys Met Leu Lys Met Gln Met Leu Glu Asp Glu
 4340 4345 4350

Asp Asp Leu Ala Tyr Ala Glu Thr Glu Lys Lys Thr Arg Thr Asp
 4355 4360 4365

Ser Thr Ser Asp Gly Arg Pro Ala Trp Met Arg Thr Leu His Thr
 4370 4375 4380

Thr Ala Ser Asn Trp Leu His Leu Ile Pro Gln Thr Leu Ser His
 4385 4390 4395

Protein Complexes associated with APP-processing

Leu Lys Arg Thr Val Glu Asn Ile Lys Asp Pro Leu Phe Arg Phe
 4400 4405 4410
 Phe Glu Arg Glu Val Lys Met Gly Ala Lys Leu Leu Gln Asp Val
 4415 4420 4425
 Arg Gln Asp Leu Ala Asp Val Val Gln Val Cys Glu Gly Lys Lys
 4430 4435 4440
 Lys Gln Thr Asn Tyr Leu Arg Thr Leu Ile Asn Glu Leu Val Lys
 4445 4450 4455
 Gly Ile Leu Pro Arg Ser Trp Ser His Tyr Thr Val Pro Ala Gly
 4460 4465 4470
 Met Thr Val Ile Gln Trp Val Ser Asp Phe Ser Glu Arg Ile Lys
 4475 4480 4485
 Gln Leu Gln Asn Ile Ser Leu Ala Ala Ala Ser Gly Gly Ala Lys
 4490 4495 4500
 Glu Leu Lys Asn Ile His Val Cys Leu Gly Gly Leu Phe Val Pro
 4505 4510 4515
 Glu Ala Tyr Ile Thr Ala Thr Arg Gln Tyr Val Ala Gln Ala Asn
 4520 4525 4530
 Ser Trp Ser Leu Glu Glu Leu Cys Leu Glu Val Asn Val Thr Thr
 4535 4540 4545
 Ser Gln Gly Ala Thr Leu Asp Ala Cys Ser Phe Gly Val Thr Gly
 4550 4555 4560
 Leu Lys Leu Gln Gly Ala Thr Cys Asn Asn Asn Lys Leu Ser Leu
 4565 4570 4575
 Ser Asn Ala Ile Ser Thr Ala Leu Pro Leu Thr Gln Leu Arg Trp
 4580 4585 4590
 Val Lys Gln Thr Asn Thr Glu Lys Lys Ala Ser Val Val Thr Leu
 4595 4600 4605
 Pro Val Tyr Leu Asn Phe Thr Arg Ala Asp Leu Ile Phe Thr Val
 4610 4615 4620
 Asp Phe Glu Ile Ala Thr Lys Glu Asp Pro Arg Ser Phe Tyr Glu
 4625 4630 4635
 Arg Gly Val Ala Val Leu Cys Thr Glu
 4640 4645

Protein Complexes associated with APP-processing

<210> 69

<211> 1524

<212> PRT

<213> Homo sapiens

<400> 69

Met Met Glu Asn His Val Ser Gln Ala Ser Val Thr Ile Arg Ile Ala
 1 5 10 15

Asp Lys Glu Val Thr Ile Lys Val Pro Ala Gly Thr Arg Leu Leu Ser
 20 25 30

Gln Pro Cys Ala Ser Asp Arg Phe Ile Gln Thr Leu Ser His Lys Gln
 35 40 45

Leu Gln Ala Glu Met Met Gln Ser His Met Val Lys Asp Ile Cys Leu
 50 55 60

Ile Gly Gly Lys Gly Cys Gly Lys Thr Val Ile Ala Lys Asn Phe Ala
 65 70 75 80

Asp Thr Leu Gly Tyr Asn Ile Glu Pro Ile Met Leu Tyr Gln Asp Met
 85 90 95

Thr Ala Arg Asp Leu Leu Gln Gln Arg Tyr Thr Leu Pro Asn Gly Asp
 100 105 110

Thr Ala Trp Arg Ser Ser Pro Leu Val Asn Ala Ala Leu Glu Gly Lys
 115 120 125

Leu Val Leu Leu Asp Gly Ile His Arg Val Asn Ala Gly Thr Leu Ala
 130 135 140

Val Leu Gln Arg Leu Ile His Asp Arg Glu Leu Ser Leu Tyr Asp Gly
 145 150 155 160

Ser Arg Leu Leu Arg Glu Asp Arg Tyr Met Arg Leu Lys Glu Glu Leu
 165 170 175

Gln Leu Ser Asp Glu Gln Leu Gln Lys Arg Ser Ile Phe Pro Ile His
 180 185 190

Pro Ser Phe Arg Ile Ile Ala Leu Ala Glu Pro Pro Val Ile Gly Ser
 195 200 205

Thr Ala His Gln Trp Leu Gly Pro Glu Phe Leu Thr Met Phe Phe Phe
 210 215 220

Protein Complexes associated with APP-processing

His Tyr Met Lys Pro Leu Val Lys Ser Glu Glu Ile Gln Val Ile Lys
 225 230 235 240

Glu Lys Val Pro Asn Val Pro Gln Glu Ala Leu Asp Lys Leu Leu Ser
 245 250 255

Phe Thr His Lys Leu Arg Glu Thr Gln Asp Pro Thr Ala Gln Ser Leu
 260 265 270

Ala Ala Ser Leu Ser Thr Arg Gln Leu Leu Arg Ile Ser Arg Arg Leu
 275 280 285

Ser Gln Tyr Pro Asn Glu Asn Leu His Ser Ala Val Thr Lys Ala Cys
 290 295 300

Leu Ser Arg Phe Leu Pro Ser Leu Ala Arg Ser Ala Leu Glu Lys Asn
 305 310 315 320

Leu Ala Asp Ala Thr Ile Glu Ile Asn Thr Asp Asp Asn Leu Glu Pro
 325 330 335

Glu Leu Lys Asp Tyr Lys Cys Glu Val Thr Ser Gly Thr Leu Arg Ile
 340 345 350

Gly Ala Val Ser Ala Pro Ile Tyr Asn Ala His Glu Lys Met Lys Val
 355 360 365

Pro Asp Val Leu Phe Tyr Asp Asn Ile Gln His Val Ile Val Met Glu
 370 375 380

Asp Met Leu Lys Asp Phe Leu Leu Gly Glu His Leu Leu Leu Val Gly
 385 390 395 400

Asn Gln Gly Val Gly Lys Asn Lys Ile Val Asp Arg Phe Leu His Leu
 405 410 415

Leu Asn Arg Pro Arg Glu Tyr Ile Gln Leu His Arg Asp Thr Thr Val
 420 425 430

Gln Thr Leu Thr Leu Gln Pro Ser Val Lys Asp Gly Leu Ile Val Tyr
 435 440 445

Glu Asp Ser Pro Leu Val Lys Ala Val Lys Leu Gly His Ile Leu Val
 450 455 460

Val Asp Glu Ala Asp Lys Ala Pro Thr Asn Val Thr Cys Ile Leu Lys
 465 470 475 480

Thr Leu Val Glu Asn Gly Glu Met Ile Leu Ala Asp Gly Arg Arg Ile
 485 490 495

Protein Complexes associated with APP-processing
 Val Ala Asn Ser Ala Asn Val Asn Gly Arg Glu Asn Val Val Val Ile
 500 505 510

His Pro Asp Phe Arg Met Ile Val Leu Ala Asn Arg Pro Gly Phe Pro
 515 520 525

Phe Leu Gly Asn Asp Phe Phe Gly Thr Leu Gly Asp Ile Phe Ser Cys
 530 535 540

His Ala Val Asp Asn Pro Lys Pro His Ser Glu Leu Glu Met Leu Arg
 545 550 555 560

Gln Tyr Gly Pro Asn Val Pro Glu Pro Ile Leu Gln Lys Leu Val Ala
 565 570 575

Ala Phe Gly Glu Leu Arg Ser Leu Ala Asp Gln Gly Ile Ile Asn Tyr
 580 585 590

Pro Tyr Ser Thr Arg Glu Val Val Asn Ile Val Lys His Leu Gln Lys
 595 600 605

Phe Pro Thr Glu Gly Leu Ser Ser Val Val Arg Asn Val Phe Asp Phe
 610 615 620

Asp Ser Tyr Asn Asn Asp Met Arg Glu Ile Leu Ile Asn Thr Leu His
 625 630 635 640

Lys Tyr Gly Ile Pro Ile Gly Ala Lys Pro Thr Ser Val Gln Leu Ala
 645 650 655

Lys Glu Leu Thr Leu Pro Glu Gln Thr Phe Met Gly Tyr Trp Thr Ile
 660 665 670

Gly Gln Ala Arg Ser Gly Met Gln Lys Leu Leu Cys Pro Val Glu Thr
 675 680 685

His His Ile Asp Ile Lys Gly Pro Ala Leu Ile Asn Ile Gln Glu Tyr
 690 695 700

Pro Ile Glu Arg His Glu Glu Arg Ser Leu Asn Phe Thr Glu Glu Cys
 705 710 715 720

Ala Ser Trp Arg Ile Pro Leu Asp Glu Ile Asn Ile Ile Cys Asp Ile
 725 730 735

Ala Thr Ser His Glu Asn Glu Gln Asn Thr Leu Tyr Val Val Thr Cys
 740 745 750

Asn Pro Ala Ser Leu Tyr Phe Met Asn Met Thr Gly Lys Ser Gly Phe
 755 760 765

Protein Complexes associated with APP-processing

Phe Val Asp Phe Phe Asp Ile Phe Pro Arg Thr Ala Asn Gly Val Trp
 770 775 780
 His Pro Phe Val Thr Val Ala Pro Leu Gly Ser Pro Leu Lys Gly Gln
 785 790 795 800
 Val Val Leu His Glu Gln Gln Ser Asn Val Ile Leu Leu Leu Asp Thr
 805 810 815
 Thr Gly Arg Ala Leu His Arg Leu Ile Leu Pro Ser Glu Lys Phe Thr
 820 825 830
 Ser Lys Lys Pro Phe Trp Trp Asn Lys Glu Glu Ala Glu Thr Tyr Lys
 835 840 845
 Met Cys Lys Glu Phe Ser His Lys Asn Trp Leu Val Phe Tyr Lys Glu
 850 855 860
 Lys Gly Asn Ser Leu Thr Val Leu Asp Val Leu Glu Gly Arg Thr His
 865 870 875 880
 Thr Ile Ser Leu Pro Ile Asn Leu Lys Thr Val Phe Leu Val Ala Glu
 885 890 895
 Asp Lys Trp Leu Leu Val Glu Ser Lys Thr Asn Gln Lys Tyr Leu Leu
 900 905 910
 Thr Lys Pro Ala His Ile Glu Ser Glu Gly Ser Gly Val Cys Gln Leu
 915 920 925
 Tyr Val Leu Lys Glu Glu Pro Pro Ser Thr Gly Phe Gly Val Thr Gln
 930 935 940
 Glu Thr Glu Phe Ser Ile Pro His Lys Ile Ser Ser Asp Gln Leu Ser
 945 950 955 960
 Ser Glu His Leu Ser Ser Ala Val Glu Gln Lys Ile Ala Ser Pro Asn
 965 970 975
 Arg Ile Leu Ser Asp Glu Lys Asn Tyr Ala Thr Ile Val Val Gly Phe
 980 985 990
 Pro Asp Leu Met Ser Pro Ser Glu Val Tyr Ser Trp Lys Arg Pro Ser
 995 1000 1005
 Ser Leu His Lys Arg Ser Gly Thr Asp Thr Ser Phe Tyr Arg Gly
 1010 1015 1020
 Lys Lys Lys Arg Gly Thr Pro Lys Gln Ser Asn Cys Val Thr Leu
 1025 1030 1035

Protein Complexes associated with APP-processing

Leu Asp Thr Asn Gln Val Val Arg Ile Leu Pro Pro Gly Glu Val
 1040 1045 1050

Pro Leu Lys Asp Ile Tyr Pro Lys Asp Val Thr Pro Pro Gln Thr
 1055 1060 1065

Ser Gly Tyr Ile Glu Val Thr Asp Leu Gln Ser Lys Lys Leu Arg
 1070 1075 1080

Tyr Ile Pro Ile Pro Arg Ser Glu Ser Leu Ser Pro Tyr Thr Thr
 1085 1090 1095

Trp Leu Ser Thr Ile Ser Asp Thr Asp Ala Leu Leu Ala Glu Trp
 1100 1105 1110

Asp Lys Ser Gly Val Val Thr Val Asp Met Gly Gly His Ile Arg
 1115 1120 1125

Leu Trp Glu Thr Gly Leu Glu Arg Leu Gln Arg Ser Leu Met Glu
 1130 1135 1140

Trp Arg Asn Met Ile Gly Gln Asp Asp Arg Asn Met Gln Ile Thr
 1145 1150 1155

Ile Asn Arg Asp Ser Gly Glu Asp Val Ser Ser Pro Lys His Gly
 1160 1165 1170

Lys Glu Asp Pro Asp Asn Met Pro His Val Gly Gly Asn Thr Trp
 1175 1180 1185

Ala Gly Gly Thr Gly Gly Arg Asp Thr Ala Gly Leu Gly Gly Lys
 1190 1195 1200

Gly Gly Pro Tyr Arg Leu Asp Ala Gly His Thr Val Tyr Gln Val
 1205 1210 1215

Ser Gln Ala Glu Lys Asp Ala Val Pro Glu Glu Val Lys Arg Ala
 1220 1225 1230

Ala Arg Glu Met Gly Gln Arg Ala Phe Gln Gln Arg Leu Lys Glu
 1235 1240 1245

Ile Gln Met Ser Glu Tyr Asp Ala Ala Thr Tyr Glu Arg Phe Ser
 1250 1255 1260

Gly Ala Val Arg Arg Gln Val His Ser Leu Arg Ile Ile Leu Asp
 1265 1270 1275

Asn Leu Gln Ala Lys Gly Lys Glu Arg Gln Trp Leu Arg His Gln
 1280 1285 1290

Protein Complexes associated with APP-processing

Ala Thr Gly Glu Leu Asp Asp Ala Lys Ile Ile Asp Gly Leu Thr
 1295 1300 1305

Gly Glu Lys Ala Ile Tyr Lys Arg Arg Gly Glu Leu Glu Pro Gln
 1310 1315 1320

Leu Gly Ser Pro Gln Gln Lys Pro Lys Arg Leu Arg Leu Val Val
 1325 1330 1335

Asp Val Ser Gly Ser Met Tyr Arg Phe Asn Arg Met Asp Gly Arg
 1340 1345 1350

Leu Glu Arg Thr Met Glu Ala Val Cys Met Val Met Glu Ala Phe
 1355 1360 1365

Glu Asn Tyr Glu Glu Lys Phe Gln Tyr Asp Ile Val Gly His Ser
 1370 1375 1380

Gly Asp Gly Tyr Asn Ile Gly Leu Val Pro Met Asn Lys Ile Pro
 1385 1390 1395

Lys Asp Asn Lys Gln Arg Leu Glu Ile Leu Lys Thr Met His Ala
 1400 1405 1410

His Ser Gln Phe Cys Met Ser Gly Asp His Thr Leu Glu Gly Thr
 1415 1420 1425

Glu His Ala Ile Lys Glu Ile Val Lys Glu Glu Ala Asp Glu Tyr
 1430 1435 1440

Phe Val Ile Val Leu Ser Asp Ala Asn Leu Ser Arg Tyr Gly Ile
 1445 1450 1455

His Pro Ala Lys Phe Ala Gln Ile Leu Thr Arg Asp Pro Gln Val
 1460 1465 1470

Asn Ala Phe Ala Ile Phe Ile Gly Ser Leu Gly Asp Gln Ala Thr
 1475 1480 1485

Arg Leu Gln Arg Thr Leu Pro Ala Gly Arg Ser Phe Val Ala Met
 1490 1495 1500

Asp Thr Lys Asp Ile Pro Gln Ile Leu Gln Gln Ile Phe Thr Ser
 1505 1510 1515

Thr Met Leu Ser Ser Val
 1520

<210> 70

<211> 841

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 70

Met Leu Glu Arg Lys Tyr Gly Gly Arg Leu Val Thr Arg His Ala Ala
 1 5 10 15

Arg Thr Ile Gln Thr Ala Phe Arg Gln Tyr Gln Met Asn Lys Asn Phe
 20 25 30

Glu Arg Leu Arg Ser Ser Met Ser Glu Asn Arg Met Ser Arg Arg Ile
 35 40 45

Val Leu Ser Asn Met Arg Met Gln Phe Ser Phe Glu Gly Pro Glu Lys
 50 55 60

Val His Ser Ser Tyr Phe Glu Gly Lys Gln Val Ser Val Thr Asn Asp
 65 70 75 80

Gly Ser Gln Leu Gly Ala Leu Val Ser Pro Glu Cys Gly Asp Leu Ser
 85 90 95

Glu Pro Thr Thr Leu Lys Ser Pro Ala Pro Ser Ser Asp Phe Ala Asp
 100 105 110

Ala Ile Thr Glu Leu Glu Asp Ala Phe Ser Arg Gln Val Lys Ser Leu
 115 120 125

Ala Glu Ser Ile Asp Asp Ala Leu Asn Cys Arg Ser Leu His Thr Glu
 130 135 140

Glu Ala Pro Ala Leu Asp Ala Ala Arg Ala Arg Asp Thr Glu Pro Gln
 145 150 155 160

Thr Ala Leu His Gly Met Asp His Arg Lys Leu Asp Glu Met Thr Ala
 165 170 175

Ser Tyr Ser Asp Val Thr Leu Tyr Ile Asp Glu Glu Glu Leu Ser Pro
 180 185 190

Pro Leu Pro Leu Ser Gln Ala Gly Asp Arg Pro Ser Ser Thr Glu Ser
 195 200 205

Asp Leu Arg Leu Arg Ala Gly Gly Ala Ala Pro Asp Tyr Trp Ala Leu
 210 215 220

Ala His Lys Glu Asp Lys Ala Asp Thr Asp Thr Ser Cys Arg Ser Thr
 225 230 235 240

Protein Complexes associated with APP-processing

Pro Ser Leu Glu Arg Gln Glu Gln Arg Leu Arg Val Glu His Leu Pro
 245 250 255

Leu Leu Thr Ile Glu Pro Pro Ser Asp Ser Ser Val Asp Leu Ser Asp
 260 265 270

Arg Ser Glu Arg Gly Ser Leu Lys Arg Gln Ser Ala Tyr Glu Arg Ser
 275 280 285

Leu Gly Gly Gln Gln Gly Ser Pro Lys His Gly Pro His Ser Gly Ala
 290 295 300

Pro Lys Ser Leu Pro Arg Glu Glu Pro Glu Leu Arg Pro Arg Pro Pro
 305 310 315 320

Arg Pro Leu Asp Ser His Leu Ala Ile Asn Gly Ser Ala Asn Arg Gln
 325 330 335

Ser Lys Ser Glu Ser Asp Tyr Ser Asp Gly Asp Asn Asp Ser Ile Asn
 340 345 350

Ser Thr Ser Asn Ser Asn Asp Thr Ile Asn Cys Ser Ser Glu Ser Ser
 355 360 365

Ser Arg Asp Ser Leu Arg Glu Gln Thr Leu Ser Lys Gln Thr Tyr His
 370 375 380

Lys Glu Ala Arg Asn Ser Trp Asp Ser Pro Ala Phe Ser Asn Asp Val
 385 390 395 400

Ile Arg Lys Arg His Tyr Arg Ile Gly Leu Asn Leu Phe Asn Lys Lys
 405 410 415

Pro Glu Lys Gly Val Gln Tyr Leu Ile Glu Arg Gly Phe Val Pro Asp
 420 425 430

Thr Pro Val Gly Val Ala His Phe Leu Leu Gln Arg Lys Gly Leu Ser
 435 440 445

Arg Gln Met Ile Gly Glu Phe Leu Gly Asn Arg Gln Lys Gln Phe Asn
 450 455 460

Arg Asp Val Leu Asp Cys Val Val Asp Glu Met Asp Phe Ser Thr Met
 465 470 475 480

Glu Leu Asp Glu Ala Leu Arg Lys Phe Gln Ala His Ile Arg Val Gln
 485 490 495

Gly Glu Ala Gln Lys Val Glu Arg Leu Ile Glu Ala Phe Ser Gln Arg
 500 505 510

Protein Complexes associated with APP-processing
 Tyr Cys Ile Cys Asn Pro Gly Val Val Arg Gln Phe Arg Asn Pro Asp
 515 520 525

Thr Ile Phe Ile Leu Ala Phe Ala Ile Ile Leu Leu Asn Thr Asp Met
 530 535 540

Tyr Ser Pro Asn Val Lys Pro Glu Arg Lys Met Lys Leu Glu Asp Phe
 545 550 555 560

Ile Lys Asn Leu Arg Gly Val Asp Asp Gly Glu Asp Ile Pro Arg Glu
 565 570 575

Met Leu Met Gly Ile Tyr Glu Arg Ile Arg Lys Arg Glu Leu Lys Thr
 580 585 590

Asn Glu Asp His Val Ser Gln Val Gln Lys Val Glu Lys Leu Ile Val
 595 600 605

Gly Lys Lys Pro Ile Gly Ser Leu His Pro Gly Leu Gly Cys Val Leu
 610 615 620

Ser Leu Pro His Arg Arg Leu Val Cys Tyr Cys Arg Leu Phe Glu Val
 625 630 635 640

Pro Asp Pro Asn Lys Pro Gln Lys Leu Gly Leu His Gln Arg Glu Ile
 645 650 655

Phe Leu Phe Asn Asp Leu Leu Val Val Thr Lys Ile Phe Gln Lys Lys
 660 665 670

Lys Asn Ser Val Thr Tyr Ser Phe Arg Gln Ser Phe Ser Leu Tyr Gly
 675 680 685

Met Gln Val Leu Leu Phe Glu Asn Gln Tyr Tyr Pro Asn Gly Ile Arg
 690 695 700

Leu Thr Ser Ser Val Pro Gly Ala Asp Ile Lys Val Leu Ile Asn Phe
 705 710 715 720

Asn Ala Pro Asn Pro Gln Asp Arg Lys Lys Phe Thr Asp Asp Leu Arg
 725 730 735

Glu Ser Ile Ala Glu Val Gln Glu Met Glu Lys His Arg Ile Glu Ser
 740 745 750

Glu Leu Glu Lys Gln Lys Gly Val Val Arg Pro Ser Met Ser Gln Cys
 755 760 765

Ser Ser Leu Lys Lys Glu Ser Gly Asn Gly Thr Leu Ser Arg Ala Cys
 770 775 780

Protein Complexes associated with APP-processing

Leu Asp Asp Ser Tyr Ala Ser Gly Glu Gly Leu Lys Arg Ser Ala Leu
 785 790 795 800

Ser Ser Ser Leu Arg Asp Leu Ser Glu Ala Gly Lys Arg Gly Arg Arg
 805 810 815

Ser Ser Ala Gly Ser Leu Glu Ser Asn Val Glu Phe Gln Pro Phe Glu
 820 825 830

Pro Leu Gln Pro Ser Val Leu Cys Ser
 835 840

<210> 71

<211> 581

<212> PRT

<213> Homo sapiens

<400> 71

Met Pro Leu Lys His Tyr Leu Leu Leu Leu Val Gly Cys Gln Ala Trp
 1 5 10 15

Gly Ala Gly Leu Ala Tyr His Gly Cys Pro Ser Glu Cys Thr Cys Ser
 20 25 30

Arg Ala Ser Gln Val Glu Cys Thr Gly Ala Arg Ile Val Ala Val Pro
 35 40 45

Thr Pro Leu Pro Trp Asn Ala Met Ser Leu Gln Ile Leu Asn Thr His
 50 55 60

Ile Thr Glu Leu Asn Glu Ser Pro Phe Leu Asn Ile Ser Ala Leu Ile
 65 70 75 80

Ala Leu Arg Ile Glu Lys Asn Glu Leu Ser Arg Ile Thr Pro Gly Ala
 85 90 95

Phe Arg Asn Leu Gly Ser Leu Arg Tyr Leu Ser Leu Ala Asn Asn Lys
 100 105 110

Leu Gln Val Leu Pro Ile Gly Leu Phe Gln Gly Leu Asp Ser Leu Glu
 115 120 125

Ser Leu Leu Leu Ser Ser Asn Gln Leu Leu Gln Ile Gln Pro Ala His
 130 135 140

Phe Ser Gln Cys Ser Asn Leu Lys Glu Leu Gln Leu His Gly Asn His
 145 150 155 160

Protein Complexes associated with APP-processing

Leu Glu Tyr Ile Pro Asp Gly Ala Phe Asp His Leu Val Gly Leu Thr
165 170 175

Lys Leu Asn Leu Gly Lys Asn Ser Leu Thr His Ile Ser Pro Arg Val
180 185 190

Phe Gln His Leu Gly Asn Leu Gln Val Leu Arg Leu Tyr Glu Asn Arg
195 200 205

Leu Thr Asp Ile Pro Met Gly Thr Phe Asp Gly Leu Val Asn Leu Gln
210 215 220

Glu Leu Ala Leu Gln Gln Asn Gln Ile Gly Leu Leu Ser Pro Gly Leu
225 230 235 240

Phe His Asn Asn His Asn Leu Gln Arg Leu Tyr Leu Ser Asn Asn His
245 250 255

Ile Ser Gln Leu Pro Pro Ser Ile Phe Met Gln Leu Pro Gln Leu Asn
260 265 270

Arg Leu Thr Leu Phe Gly Asn Ser Leu Lys Glu Leu Ser Leu Gly Ile
275 280 285

Phe Gly Pro Met Pro Asn Leu Arg Glu Leu Trp Leu Tyr Asp Asn His
290 295 300

Ile Ser Ser Leu Pro Asp Asn Val Phe Ser Asn Leu Arg Gln Leu Gln
305 310 315 320

Val Leu Ile Leu Ser Arg Asn Gln Ile Ser Phe Ile Ser Pro Gly Ala
325 330 335

Phe Asn Gly Leu Thr Glu Leu Arg Glu Leu Ser Leu His Thr Asn Ala
340 345 350

Leu Gln Asp Leu Asp Gly Asn Val Phe Arg Met Leu Ala Asn Leu Gln
355 360 365

Asn Ile Ser Leu Gln Asn Asn Arg Leu Arg Gln Leu Pro Gly Asn Ile
370 375 380

Phe Ala Asn Val Asn Gly Leu Met Ala Ile Gln Leu Gln Asn Asn Gln
385 390 395 400

Leu Glu Asn Leu Pro Leu Gly Ile Phe Asp His Leu Gly Lys Leu Cys
405 410 415

Glu Leu Arg Leu Tyr Asp Asn Pro Trp Arg Cys Asp Ser Asp Ile Leu
420 425 430

Protein Complexes associated with APP-processing

Pro Leu Arg Asn Trp Leu Leu Leu Asn Gln Pro Arg Leu Gly Thr Asp
 435 440 445

Thr Val Pro Val Cys Phe Ser Pro Ala Asn Val Arg Gly Gln Ser Leu
 450 455 460

Ile Ile Ile Asn Val Asn Val Ala Val Pro Ser Val His Val Pro Glu
 465 470 475 480

Val Pro Ser Tyr Pro Glu Thr Pro Trp Tyr Pro Asp Thr Pro Ser Tyr
 485 490 495

Pro Asp Thr Thr Ser Val Ser Ser Thr Thr Glu Leu Thr Ser Pro Val
 500 505 510

Glu Asp Tyr Thr Asp Leu Thr Thr Ile Gln Val Thr Asp Asp Arg Ser
 515 520 525

Val Trp Gly Met Thr His Ala His Ser Gly Leu Ala Ile Ala Ala Ile
 530 535 540

Val Ile Gly Ile Val Ala Leu Ala Cys Ser Leu Ala Ala Cys Val Gly
 545 550 555 560

Cys Cys Cys Cys Lys Lys Arg Ser Gln Ala Val Leu Met Gln Met Lys
 565 570 575

Ala Pro Asn Glu Cys
 580

<210> 72

<211> 1609

<212> PRT

<213> Homo sapiens

<400> 72

Met Arg Gly Ser His Arg Ala Ala Pro Ala Leu Arg Pro Arg Gly Arg
 1 5 10 15

Leu Trp Pro Val Leu Ala Val Leu Ala Ala Ala Ala Ala Gly Cys
 20 25 30

Ala Gln Ala Ala Met Asp Glu Cys Thr Asp Glu Gly Gly Arg Pro Gln
 35 40 45

Arg Cys Met Pro Glu Phe Val Asn Ala Ala Phe Asn Val Thr Val Val
 50 55 60

Protein Complexes associated with APP-processing

Ala Thr Asn Thr Cys Gly Thr Pro Pro Glu Glu Tyr Cys Val Gln Thr
65 70 75 80

Gly Val Thr Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly Gln
85 90 95

Pro His Leu Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn Gln
100 105 110

Ala Asp Thr Thr Trp Trp Gln Ser Gln Thr Met Leu Ala Gly Val Gln
115 120 125

Tyr Pro Ser Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe Asp
130 135 140

Ile Thr Tyr Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser Phe
145 150 155 160

Ala Ile Tyr Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr Gln
165 170 175

Tyr Tyr Ser Gly Ser Cys Glu Asn Thr Tyr Ser Lys Ala Asn Arg Gly
180 185 190

Phe Ile Arg Thr Gly Gly Asp Glu Gln Gln Ala Leu Cys Thr Asp Glu
195 200 205

Phe Ser Asp Phe Ser Pro Leu Thr Gly Gly Asn Val Ala Phe Ser Thr
210 215 220

Leu Glu Gly Arg Pro Ser Ala Tyr Asn Phe Asp Asn Ser Pro Val Leu
225 230 235 240

Gln Glu Trp Val Thr Ala Thr Asp Ile Arg Val Thr Leu Asn Arg Leu
245 250 255

Asn Thr Phe Gly Asp Glu Val Phe Asn Asp Pro Lys Val Leu Lys Ser
260 265 270

Tyr Tyr Tyr Ala Ile Ser Asp Phe Ala Val Gly Gly Arg Cys Lys Cys
275 280 285

Asn Gly His Ala Ser Glu Cys Met Lys Asn Glu Phe Asp Lys Leu Val
290 295 300

Cys Asn Cys Lys His Asn Thr Tyr Gly Val Asp Cys Glu Lys Cys Leu
305 310 315 320

Pro Phe Phe Asn Asp Arg Pro Trp Arg Arg Ala Thr Ala Glu Ser Ala
325 330 335

Protein Complexes associated with APP-processing

Ser Glu Cys Leu Pro Cys Asp Cys Asn Gly Arg Ser Gln Glu Cys Tyr
 340 345 350

Phe Asp Pro Glu Leu Tyr Arg Ser Thr Gly His Gly Gly His Cys Thr
 355 360 365

Asn Cys Gln Asp Asn Thr Asp Gly Ala His Cys Glu Arg Cys Arg Glu
 370 375 380

Asn Phe Phe Arg Leu Gly Asn Asn Glu Ala Cys Ser Ser Cys His Cys
 385 390 395 400

Ser Pro Val Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg Cys
 405 410 415

Ser Cys Lys Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln Pro
 420 425 430

Gly Phe His Ser Leu Thr Glu Ala Gly Cys Arg Pro Cys Ser Cys Asp
 435 440 445

Pro Ser Gly Ser Ile Asp Glu Cys Asn Val Glu Thr Gly Arg Cys Val
 450 455 460

Cys Lys Asp Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro Gly
 465 470 475 480

Phe Phe Asn Leu Glu Ser Ser Asn Pro Arg Gly Cys Thr Pro Cys Phe
 485 490 495

Cys Phe Gly His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser Val
 500 505 510

Tyr Ser Ile Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg Ala
 515 520 525

Glu Gln Arg Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Glu Arg
 530 535 540

Gln Asp Ile Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe Ile
 545 550 555 560

Ala Pro Ala Lys Phe Leu Gly Lys Gln Val Leu Ser Tyr Gly Gln Asn
 565 570 575

Leu Ser Phe Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser Ala
 580 585 590

Glu Asp Leu Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro Leu
 595 600 605

Protein Complexes associated with APP-processing

Ile Ala Gln Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr Val
610 615 620

Phe Arg Leu His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu Thr
625 630 635 640

Pro Phe Glu Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys Ile
645 650 655

Arg Gly Thr Tyr Ser Glu Arg Ser Ala Gly Tyr Leu Asp Asp Val Thr
660 665 670

Leu Ala Ser Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val Glu
675 680 685

Ser Cys Thr Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Met Cys
690 695 700

Leu Ser Gly Tyr Arg Arg Glu Thr Pro Asn Leu Gly Pro Tyr Ser Pro
705 710 715 720

Cys Val Leu Cys Ala Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu
725 730 735

Thr Gly Val Cys Asn Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu
740 745 750

Lys Cys Ser Asp Gly Tyr Tyr Gly Asp Ser Thr Ala Gly Thr Ser Ser
755 760 765

Asp Cys Gln Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Val Val
770 775 780

Pro Lys Thr Lys Glu Val Val Cys Thr Asn Cys Pro Thr Gly Thr Thr
785 790 795 800

Gly Lys Arg Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu
805 810 815

Gly Arg Asn Gly Pro Val Arg Leu Cys Arg Leu Cys Gln Cys Ser Asp
820 825 830

Asn Ile Asp Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly Glu
835 840 845

Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg Cys
850 855 860

Lys Asp Gly Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp Lys
865 870 875 880

Protein Complexes associated with APP-processing
 Cys Lys Ala Cys Asn Cys Asn Pro Tyr Gly Thr Met Lys Gln Gln Ser
 885 890 895

Ser Cys Asn Pro Val Thr Gly Gln Cys Glu Cys Leu Pro His Val Thr
 900 905 910

Gly Gln Asp Cys Gly Ala Cys Asp Pro Gly Phe Tyr Asn Leu Gln Ser
 915 920 925

Gly Gln Gly Cys Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn
 930 935 940

Gly Gln Cys Asp Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile
 945 950 955 960

Thr Gly Gln His Cys Glu Arg Cys Glu Val Asn His Phe Gly Phe Gly
 965 970 975

Pro Glu Gly Cys Lys Pro Cys Asp Cys His Pro Glu Gly Ser Leu Ser
 980 985 990

Leu Gln Cys Lys Asp Asp Gly Arg Cys Glu Cys Arg Glu Gly Phe Val
 995 1000 1005

Gly Asn Arg Cys Asp Gln Cys Glu Glu Asn Tyr Phe Tyr Asn Arg
 1010 1015 1020

Ser Trp Pro Gly Cys Gln Glu Cys Pro Ala Cys Tyr Arg Leu Val
 1025 1030 1035

Lys Asp Lys Val Ala Asp His Arg Val Lys Leu Gln Glu Leu Glu
 1040 1045 1050

Ser Leu Ile Ala Asn Leu Gly Thr Gly Asp Glu Met Val Thr Asp
 1055 1060 1065

Gln Ala Phe Glu Asp Arg Leu Lys Glu Ala Glu Arg Glu Val Met
 1070 1075 1080

Asp Leu Leu Arg Glu Ala Gln Asp Val Lys Asp Val Asp Gln Asn
 1085 1090 1095

Leu Met Asp Arg Leu Gln Arg Val Asn Asn Thr Leu Ser Ser Gln
 1100 1105 1110

Ile Ser Arg Leu Gln Asn Ile Arg Asn Thr Ile Glu Glu Thr Gly
 1115 1120 1125

Asn Leu Ala Glu Gln Ala Arg Ala His Val Glu Asn Thr Glu Arg
 1130 1135 1140

Protein Complexes associated with APP-processing

Leu Ile Glu Ile Ala Ser Arg Glu Leu Glu Lys Ala Lys Val Ala
 1145 1150 1155

Ala Ala Asn Val Ser Val Thr Gln Pro Glu Ser Thr Gly Asp Pro
 1160 1165 1170

Asn Asn Met Thr Leu Leu Ala Glu Glu Ala Arg Lys Leu Ala Glu
 1175 1180 1185

Arg His Lys Gln Glu Ala Asp Asp Ile Val Arg Val Ala Lys Thr
 1190 1195 1200

Ala Asn Asp Thr Ser Thr Glu Ala Tyr Asn Leu Leu Leu Arg Thr
 1205 1210 1215

Leu Ala Gly Glu Asn Gln Thr Ala Phe Glu Ile Glu Glu Leu Asn
 1220 1225 1230

Arg Lys Tyr Glu Gln Ala Lys Asn Ile Ser Gln Asp Leu Glu Lys
 1235 1240 1245

Gln Ala Ala Arg Val His Glu Glu Ala Lys Arg Ala Gly Asp Lys
 1250 1255 1260

Ala Val Glu Ile Tyr Ala Ser Val Ala Gln Leu Ser Pro Leu Asp
 1265 1270 1275

Ser Glu Thr Leu Glu Asn Glu Ala Asn Asn Ile Lys Met Glu Ala
 1280 1285 1290

Glu Asn Leu Glu Gln Leu Ile Asp Gln Lys Leu Lys Asp Tyr Glu
 1295 1300 1305

Asp Leu Arg Glu Asp Met Arg Gly Lys Glu Leu Glu Val Lys Asn
 1310 1315 1320

Leu Leu Glu Lys Gly Lys Thr Glu Gln Gln Thr Ala Asp Gln Leu
 1325 1330 1335

Leu Ala Arg Ala Asp Ala Ala Lys Ala Leu Ala Glu Glu Ala Ala
 1340 1345 1350

Lys Lys Gly Arg Asp Thr Leu Gln Glu Ala Asn Asp Ile Leu Asn
 1355 1360 1365

Asn Leu Lys Asp Phe Asp Arg Arg Val Asn Asp Asn Lys Thr Ala
 1370 1375 1380

Ala Glu Glu Ala Leu Arg Lys Ile Pro Ala Ile Asn Gln Thr Ile
 1385 1390 1395

Protein Complexes associated with APP-processing

Thr Glu Ala Asn Glu Lys Thr Arg Glu Ala Gln Gln Ala Leu Gly
 1400 1405 1410

 Ser Ala Ala Ala Asp Ala Thr Glu Ala Lys Asn Lys Ala His Glu
 1415 1420 1425

 Ala Glu Arg Ile Ala Ser Ala Val Gln Lys Asn Ala Thr Ser Thr
 1430 1435 1440

 Lys Ala Glu Ala Glu Arg Thr Phe Ala Glu Val Thr Asp Leu Asp
 1445 1450 1455

 Asn Glu Val Asn Asn Met Leu Lys Gln Leu Gln Glu Ala Glu Lys
 1460 1465 1470

 Glu Leu Lys Arg Lys Gln Asp Asp Ala Asp Gln Asp Met Met Met
 1475 1480 1485

 Ala Gly Met Ala Ser Gln Ala Ala Gln Glu Ala Glu Ile Asn Ala
 1490 1495 1500

 Arg Lys Ala Lys Asn Ser Val Thr Ser Leu Leu Ser Ile Ile Asn
 1505 1510 1515

 Asp Leu Leu Glu Gln Leu Gly Gln Leu Asp Thr Val Asp Leu Asn
 1520 1525 1530

 Lys Leu Asn Glu Ile Glu Gly Thr Leu Asn Lys Ala Lys Asp Glu
 1535 1540 1545

 Met Lys Val Ser Asp Leu Asp Arg Lys Val Ser Asp Leu Glu Asn
 1550 1555 1560

 Glu Ala Lys Lys Gln Glu Ala Ala Ile Met Asp Tyr Asn Arg Asp
 1565 1570 1575

 Ile Glu Glu Ile Met Lys Asp Ile Arg Asn Leu Glu Asp Ile Arg
 1580 1585 1590

 Lys Thr Leu Pro Ser Gly Cys Phe Asn Thr Pro Ser Ile Glu Lys
 1595 1600 1605

Pro

<210> 73

<211> 344

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 73

Met Ala Ala Ala Thr Glu His Asn Arg Pro Ser Ser Gly Asp Arg Asn
 1 5 10 15

Leu Glu Arg Arg Cys Ser Pro Asn Leu Ser Arg Glu Val Leu Tyr Glu
 20 25 30

Ile Phe Arg Ser Leu His Thr Leu Val Gly Gln Leu Asp Leu Arg Asp
 35 40 45

Asp Val Val Lys Ile Thr Ile Asp Trp Asn Lys Leu Gln Ser Leu Ser
 50 55 60

Ala Phe Gln Pro Ala Leu Leu Phe Ser Ala Leu Glu Gln His Ile Leu
 65 70 75 80

Tyr Leu Gln Pro Phe Leu Ala Lys Leu Gln Ser Pro Ile Lys Glu Glu
 85 90 95

Asn Thr Thr Ala Val Glu Glu Ile Gly Arg Thr Glu Met Gly Asn Lys
 100 105 110

Asn Glu Val Asn Asp Lys Phe Ser Ile Gly Asp Leu Gln Glu Glu Glu
 115 120 125

Lys His Lys Glu Ser Asp Leu Arg Asp Val Lys Lys Thr Gln Ile His
 130 135 140

Phe Asp Pro Glu Val Val Gln Ile Lys Ala Gly Lys Ala Glu Ile Asp
 145 150 155 160

Arg Arg Ile Ser Ala Phe Ile Glu Arg Lys Gln Ala Glu Ile Asn Glu
 165 170 175

Asn Asn Val Arg Glu Phe Cys Asn Val Ile Asp Cys Asn Gln Glu Asn
 180 185 190

Ser Cys Ala Arg Thr Asp Ala Ile Phe Thr Pro Tyr Pro Gly Phe Lys
 195 200 205

Ser His Val Lys Val Ser Arg Val Val Asn Thr Tyr Gly Pro Gln Thr
 210 215 220

Arg Pro Glu Gly Ile Pro Gly Ser Gly His Lys Pro Asn Ser Met Leu
 225 230 235 240

Arg Asp Cys Gly Asn Gln Ala Val Glu Glu Arg Leu Gln Asn Ile Glu
 245 250 255

Protein Complexes associated with APP-processing

Ala His Leu Arg Leu Gln Thr Gly Gly Pro Val Pro Arg Asp Ile Tyr
 260 265 270

Gln Arg Ile Lys Lys Leu Glu Asp Lys Ile Leu Glu Leu Glu Gly Ile
 275 280 285

Ser Pro Glu Tyr Phe Gln Ser Val Ser Phe Ser Gly Lys Arg Arg Lys
 290 295 300

Val Gln Pro Pro Gln Gln Asn Tyr Ser Leu Ala Glu Leu Asp Glu Lys
 305 310 315 320

Ile Ser Ala Leu Lys Gln Ala Leu Leu Arg Lys Ser Arg Glu Ala Glu
 325 330 335

Ser Met Ala Thr His His Leu Pro
 340

<210> 74

<211> 1576

<212> PRT

<213> Homo sapiens

<400> 74

Leu Cys Asn Gly Val Asn Asp Cys Gly Asp Asn Ser Asp Glu Ser Pro
 1 5 10 15

Gln Gln Asn Cys Arg Pro Arg Thr Gly Glu Glu Asn Cys Asn Val Asn
 20 25 30

Asn Gly Gly Cys Ala Gln Lys Cys Gln Met Val Arg Gly Ala Val Gln
 35 40 45

Cys Thr Cys His Thr Gly Tyr Arg Leu Thr Glu Asp Gly His Thr Cys
 50 55 60

Gln Asp Val Asn Glu Cys Ala Glu Glu Gly Tyr Cys Ser Gln Gly Cys
 65 70 75 80

Thr Asn Ser Glu Gly Ala Phe Gln Cys Trp Cys Glu Thr Gly Tyr Glu
 85 90 95

Leu Arg Pro Asp Arg Arg Ser Cys Lys Ala Leu Gly Pro Glu Pro Val
 100 105 110

Leu Leu Phe Ala Asn Arg Ile Asp Ile Arg Gln Val Leu Pro His Arg
 115 120 125

Protein Complexes associated with APP-processing

Ser Glu Tyr Thr Leu Leu Leu Asn Asn Leu Glu Asn Ala Ile Ala Leu
130 135 140

Asp Phe His His Arg Arg Glu Leu Val Phe Trp Ser Asp Val Thr Leu
145 150 155 160

Asp Arg Ile Leu Arg Ala Asn Leu Asn Gly Ser Asn Val Glu Glu Val
165 170 175

Val Ser Thr Gly Leu Glu Ser Pro Gly Gly Leu Ala Val Asp Trp Val
180 185 190

His Asp Lys Leu Tyr Trp Thr Asp Ser Gly Thr Ser Arg Ile Glu Val
195 200 205

Ala Asn Leu Asp Gly Ala His Arg Lys Val Leu Leu Trp Gln Asn Leu
210 215 220

Glu Lys Pro Arg Ala Ile Ala Leu His Pro Met Glu Gly Thr Ile Tyr
225 230 235 240

Trp Thr Asp Trp Gly Asn Thr Pro Arg Ile Glu Ala Ser Ser Met Asp
245 250 255

Gly Ser Gly Arg Arg Ile Ile Ala Asp Thr His Leu Phe Trp Pro Asn
260 265 270

Gly Leu Thr Ile Asp Tyr Ala Gly Arg Arg Met Tyr Trp Val Asp Ala
275 280 285

Lys His His Val Ile Glu Arg Ala Asn Leu Asp Gly Ser His Arg Lys
290 295 300

Ala Val Ile Ser Gln Gly Leu Pro His Pro Phe Ala Ile Thr Val Phe
305 310 315 320

Glu Asp Ser Leu Tyr Trp Thr Asp Trp His Thr Lys Ser Ile Asn Ser
325 330 335

Ala Asn Lys Phe Thr Gly Lys Asn Gln Glu Ile Ile Arg Asn Lys Leu
340 345 350

His Phe Pro Met Asp Ile His Thr Leu His Pro Gln Arg Gln Pro Ala
355 360 365

Gly Lys Asn Arg Cys Gly Asp Asn Asn Gly Gly Cys Thr His Leu Cys
370 375 380

Leu Pro Ser Gly Gln Asn Tyr Thr Cys Ala Cys Pro Thr Gly Phe Arg
385 390 395 400

Protein Complexes associated with APP-processing

Lys Ile Ser Ser His Ala Cys Ala Gln Ser Leu Asp Lys Phe Leu Leu
405 410 415

Phe Ala Arg Arg Met Asp Ile Arg Arg Ile Ser Phe Asp Thr Glu Asp
420 425 430

Leu Ser Asp Asp Val Ile Pro Leu Ala Asp Val Arg Ser Ala Val Ala
435 440 445

Leu Asp Trp Asp Ser Arg Asp Asp His Val Tyr Trp Thr Asp Val Ser
450 455 460

Thr Asp Thr Ile Ser Arg Ala Lys Trp Asp Gly Thr Gly Gln Glu Val
465 470 475 480

Val Val Asp Thr Ser Leu Glu Ser Pro Ala Gly Leu Ala Ile Asp Trp
485 490 495

Val Thr Asn Lys Leu Tyr Trp Thr Asp Ala Gly Thr Asp Arg Ile Glu
500 505 510

Val Ala Asn Thr Asp Gly Ser Met Arg Thr Val Leu Ile Trp Glu Asn
515 520 525

Leu Asp Arg Pro Arg Asp Ile Val Val Glu Pro Met Gly Gly Tyr Met
530 535 540

Tyr Trp Thr Asp Trp Gly Ala Ser Pro Lys Ile Glu Arg Ala Gly Met
545 550 555 560

Asp Ala Ser Gly Arg Gln Val Ile Ile Ser Ser Asn Leu Thr Trp Pro
565 570 575

Asn Gly Leu Ala Ile Asp Tyr Gly Ser Gln Arg Leu Tyr Trp Ala Asp
580 585 590

Ala Gly Met Lys Thr Ile Glu Phe Ala Gly Leu Asp Gly Ser Lys Arg
595 600 605

Lys Val Leu Ile Gly Ser Gln Leu Pro His Pro Phe Gly Leu Thr Leu
610 615 620

Tyr Gly Glu Arg Ile Tyr Trp Thr Asp Trp Gln Thr Lys Ser Ile Gln
625 630 635 640

Ser Ala Asp Arg Leu Thr Gly Leu Asp Arg Glu Thr Leu Gln Glu Asn
645 650 655

Leu Glu Asn Leu Met Asp Ile His Val Phe His Arg Arg Arg Pro Pro
660 665 670

Protein Complexes associated with APP-processing

Val Ser Thr Pro Cys Ala Met Glu Asn Gly Gly Cys Ser His Leu Cys
675 680 685

Leu Arg Ser Pro Asn Pro Ser Gly Phe Ser Cys Thr Cys Pro Thr Gly
690 695 700

Ile Asn Leu Leu Ser Asp Gly Lys Thr Cys Ser Pro Gly Met Asn Ser
705 710 715 720

Phe Leu Ile Phe Ala Arg Arg Ile Asp Ile Arg Met Val Ser Leu Asp
725 730 735

Ile Pro Tyr Phe Ala Asp Val Val Val Pro Ile Asn Ile Thr Met Lys
740 745 750

Asn Thr Ile Ala Val Gly Val Asp Pro Gln Glu Gly Lys Val Tyr Trp
755 760 765

Ser Asp Ser Thr Leu His Arg Ile Ser Arg Ala Asn Leu Asp Gly Ser
770 775 780

Gln His Glu Asp Ile Ile Thr Thr Gly Leu Gln Thr Thr Asp Gly Leu
785 790 795 800

Ala Val Asp Ala Ile Gly Arg Lys Val Tyr Trp Thr Asp Thr Gly Thr
805 810 815

Asn Arg Ile Glu Val Gly Asn Leu Asp Gly Ser Met Arg Lys Val Leu
820 825 830

Val Trp Gln Asn Leu Asp Ser Pro Arg Ala Ile Val Leu Tyr His Glu
835 840 845

Met Gly Phe Met Tyr Trp Thr Asp Trp Gly Glu Asn Ala Lys Leu Glu
850 855 860

Arg Ser Gly Met Asp Gly Ser Asp Arg Ala Val Leu Ile Asn Asn Asn
865 870 875 880

Leu Gly Trp Pro Asn Gly Leu Thr Val Asp Lys Ala Ser Ser Gln Leu
885 890 895

Leu Trp Ala Asp Ala His Thr Glu Arg Ile Glu Ala Ala Asp Leu Asn
900 905 910

Gly Ala Asn Arg His Thr Leu Val Ser Pro Val Gln His Pro Tyr Gly
915 920 925

Leu Thr Leu Leu Asp Ser Tyr Ile Tyr Trp Thr Asp Trp Gln Thr Arg
930 935 940

Protein Complexes associated with APP-processing

Ser Ile His Arg Ala Asp Lys Gly Thr Gly Ser Asn Val Ile Leu Val
 945 950 955 960

Arg Ser Asn Leu Pro Gly Leu Met Asp Met Gln Ala Val Asp Arg Ala
 965 970 975

Gln Pro Leu Gly Phe Asn Lys Cys Gly Ser Arg Asn Gly Gly Cys Ser
 980 985 990

His Leu Cys Leu Pro Arg Pro Ser Gly Phe Ser Cys Ala Cys Pro Thr
 995 1000 1005

Gly Ile Gln Leu Lys Gly Asp Gly Lys Thr Cys Asp Pro Ser Pro
 1010 1015 1020

Glu Thr Tyr Leu Leu Phe Ser Ser Arg Gly Ser Ile Arg Arg Ile
 1025 1030 1035

Ser Leu Asp Thr Ser Asp His Thr Asp Val His Val Pro Val Pro
 1040 1045 1050

Glu Leu Asn Asn Val Ile Ser Leu Asp Tyr Asp Ser Val Asp Gly
 1055 1060 1065

Lys Val Tyr Tyr Thr Asp Val Phe Leu Asp Val Ile Arg Arg Ala
 1070 1075 1080

Asp Leu Asn Gly Ser Asn Met Glu Thr Val Ile Gly Arg Gly Leu
 1085 1090 1095

Lys Thr Thr Asp Gly Leu Ala Val Asp Trp Val Ala Arg Asn Leu
 1100 1105 1110

Tyr Trp Thr Asp Thr Gly Arg Asn Thr Ile Glu Ala Ser Arg Leu
 1115 1120 1125

Asp Gly Ser Cys Arg Lys Val Leu Ile Asn Asn Ser Leu Asp Glu
 1130 1135 1140

Pro Arg Ala Ile Ala Val Phe Pro Arg Lys Gly Tyr Leu Phe Trp
 1145 1150 1155

Thr Asp Trp Gly His Ile Ala Lys Ile Glu Arg Ala Asn Leu Asp
 1160 1165 1170

Gly Ser Glu Arg Lys Val Leu Ile Asn Thr Asp Leu Gly Trp Pro
 1175 1180 1185

Asn Gly Leu Thr Leu Asp Tyr Asp Thr Arg Arg Ile Tyr Trp Val
 1190 1195 1200

Protein Complexes associated with APP-processing

Asp	Ala	His	Leu	Asp	Arg	Ile	Glu	Ser	Ala	Asp	Leu	Asn	Gly	Lys
1205						1210					1215			
Leu	Arg	Gln	Val	Leu	Val	Gly	His	Val	Ser	His	Pro	Phe	Ala	Leu
1220						1225					1230			
Thr	Gln	Gln	Asp	Arg	Trp	Ile	Tyr	Trp	Thr	Asp	Trp	Gln	Thr	Lys
1235						1240					1245			
Ser	Ile	Gln	Arg	Val	Asp	Lys	Tyr	Ser	Gly	Arg	Asn	Lys	Glu	Thr
1250						1255					1260			
Val	Leu	Ala	Asn	Val	Glu	Gly	Leu	Met	Asp	Ile	Ile	Val	Val	Ser
1265						1270					1275			
Pro	Gln	Arg	Gln	Thr	Gly	Thr	Asn	Ala	Cys	Gly	Val	Asn	Asn	Gly
1280						1285					1290			
Gly	Cys	Thr	His	Leu	Cys	Phe	Ala	Arg	Ala	Ser	Asp	Phe	Val	Cys
1295						1300					1305			
Ala	Cys	Pro	Asp	Glu	Pro	Asp	Ser	Gln	Pro	Cys	Ser	Leu	Val	Pro
1310						1315					1320			
Gly	Leu	Val	Pro	Pro	Ala	Pro	Arg	Ala	Thr	Gly	Met	Ser	Glu	Lys
1325						1330					1335			
Ser	Pro	Val	Leu	Pro	Asn	Thr	Pro	Pro	Thr	Thr	Leu	Tyr	Ser	Ser
1340						1345					1350			
Thr	Thr	Arg	Thr	Arg	Thr	Ser	Leu	Glu	Glu	Val	Glu	Gly	Arg	Cys
1355						1360					1365			
Ser	Glu	Arg	Asp	Ala	Arg	Leu	Gly	Leu	Cys	Ala	Arg	Ser	Asn	Asp
1370						1375					1380			
Ala	Val	Pro	Ala	Ala	Pro	Gly	Glu	Gly	Leu	His	Ile	Ser	Tyr	Ala
1385						1390					1395			
Ile	Gly	Gly	Leu	Leu	Ser	Ile	Leu	Leu	Ile	Leu	Val	Val	Ile	Ala
1400						1405					1410			
Ala	Leu	Met	Leu	Tyr	Arg	His	Lys	Lys	Ser	Lys	Phe	Thr	Asp	Pro
1415						1420					1425			
Gly	Met	Gly	Asn	Leu	Thr	Tyr	Ser	Asn	Pro	Ser	Tyr	Arg	Thr	Ser
1430						1435					1440			
Thr	Gln	Glu	Val	Lys	Ile	Glu	Ala	Ile	Pro	Lys	Pro	Ala	Met	Tyr
1445						1450					1455			

Protein Complexes associated with APP-processing
 Asn Gln Leu Cys Tyr Lys Lys Glu Gly Gly Pro Asp His Asn Tyr
 1460 1465 1470

Thr Lys Glu Lys Ile Lys Ile Val Glu Gly Ile Cys Leu Leu Ser
 1475 1480 1485

Gly Asp Asp Ala Glu Trp Asp Asp Leu Lys Gln Leu Arg Ser Ser
 1490 1495 1500

Arg Gly Gly Leu Leu Arg Asp His Val Cys Met Lys Thr Asp Thr
 1505 1510 1515

Val Ser Ile Gln Ala Ser Ser Gly Ser Leu Asp Asp Thr Glu Met
 1520 1525 1530

Glu Gln Leu Leu Gln Glu Glu Gln Ser Glu Cys Ser Ser Val His
 1535 1540 1545

Thr Ala Ala Thr Pro Glu Arg Arg Gly Ser Leu Pro Asp Thr Gly
 1550 1555 1560

Trp Lys His Glu Arg Lys Leu Ser Ser Glu Ser Gln Val
 1565 1570 1575

<210> 75

<211> 603

<212> PRT

<213> Homo sapiens

<400> 75

Met Ala Pro Ile Gly Leu Lys Ala Val Val Gly Glu Lys Ile Met His
 1 5 10 15

Asp Val Ile Lys Lys Val Lys Lys Lys Gly Glu Trp Lys Val Leu Val
 20 25 30

Val Asp Gln Leu Ser Met Arg Met Leu Ser Ser Cys Cys Lys Met Thr
 35 40 45

Asp Ile Met Thr Glu Gly Ile Thr Ile Val Glu Asp Ile Asn Lys Arg
 50 55 60

Arg Glu Pro Leu Pro Ser Leu Glu Ala Val Tyr Leu Ile Thr Pro Ser
 65 70 75 80

Glu Lys Ser Val His Ser Leu Ile Ser Asp Phe Lys Asp Pro Pro Thr
 85 90 95

Protein Complexes associated with APP-processing

Ala Lys Tyr Arg Ala Ala His Val Phe Phe Thr Asp Ser Cys Pro Asp
100 105 110

Ala Leu Phe Asn Glu Leu Val Lys Ser Arg Ala Ala Lys Val Ile Lys
115 120 125

Thr Leu Thr Glu Ile Asn Ile Ala Phe Leu Pro Tyr Glu Ser Gln Val
130 135 140

Tyr Ser Leu Asp Ser Ala Asp Ser Phe Gln Ser Phe Tyr Ser Pro His
145 150 155 160

Lys Ala Gln Met Lys Asn Pro Ile Leu Glu Arg Leu Ala Glu Gln Ile
165 170 175

Ala Thr Leu Cys Ala Thr Leu Lys Glu Tyr Pro Ala Val Arg Tyr Arg
180 185 190

Gly Glu Tyr Lys Asp Asn Ala Leu Leu Ala Gln Leu Ile Gln Asp Lys
195 200 205

Leu Asp Ala Tyr Lys Ala Asp Asp Pro Thr Met Gly Glu Gly Pro Asp
210 215 220

Lys Ala Arg Ser Gln Leu Leu Ile Leu Asp Arg Gly Phe Asp Pro Ser
225 230 235 240

Ser Pro Val Leu His Glu Leu Thr Phe Gln Ala Met Ser Tyr Asp Leu
245 250 255

Leu Pro Ile Glu Asn Asp Val Tyr Lys Tyr Glu Thr Ser Gly Ile Gly
260 265 270

Glu Ala Arg Val Lys Glu Val Leu Leu Asp Glu Asp Asp Asp Leu Trp
275 280 285

Ile Ala Leu Arg His Lys His Ile Ala Glu Val Ser Gln Glu Val Thr
290 295 300

Arg Ser Leu Lys Asp Phe Ser Ser Ser Lys Arg Met Asn Thr Gly Glu
305 310 315 320

Lys Thr Thr Met Arg Asp Leu Ser Gln Met Leu Lys Lys Met Pro Gln
325 330 335

Tyr Gln Lys Glu Leu Ser Lys Tyr Ser Thr His Leu His Leu Ala Glu
340 345 350

Asp Cys Met Lys His Tyr Gln Gly Thr Val Asp Lys Leu Cys Arg Val
355 360 365

Protein Complexes associated with APP-processing

Glu Gln Asp Leu Ala Met Gly Thr Asp Ala Glu Gly Glu Lys Ile Lys
 370 375 380

Asp Pro Met Arg Ala Ile Val Pro Ile Leu Leu Asp Ala Asn Val Ser
 385 390 395 400

Thr Tyr Asp Lys Ile Arg Ile Ile Leu Leu Tyr Ile Phe Leu Lys Asn
 405 410 415

Gly Ile Thr Glu Glu Asn Leu Asn Lys Leu Ile Gln His Ala Gln Ile
 420 425 430

Pro Pro Glu Asp Ser Glu Ile Ile Thr Asn Met Ala His Leu Gly Val
 435 440 445

Pro Ile Val Thr Asp Ser Thr Leu Arg Arg Arg Ser Lys Pro Glu Arg
 450 455 460

Lys Glu Arg Ile Ser Glu Gln Thr Tyr Gln Leu Ser Arg Trp Thr Pro
 465 470 475 480

Ile Ile Lys Asp Ile Met Glu Asp Thr Ile Glu Asp Lys Leu Asp Thr
 485 490 495

Lys His Tyr Pro Tyr Ile Ser Thr Arg Ser Ser Ala Ser Phe Ser Thr
 500 505 510

Thr Ala Val Ser Ala Arg Tyr Gly His Trp His Lys Asn Lys Ala Pro
 515 520 525

Gly Glu Tyr Arg Ser Gly Pro Arg Leu Ile Ile Phe Ile Leu Gly Gly
 530 535 540

Val Ser Leu Asn Glu Met Arg Cys Ala Tyr Glu Val Thr Gln Ala Asn
 545 550 555 560

Gly Lys Trp Glu Val Leu Ile Gly Ser Thr His Ile Leu Thr Pro Thr
 565 570 575

Lys Phe Leu Met Asp Leu Arg His Pro Asp Phe Arg Glu Ser Ser Arg
 580 585 590

Val Ser Phe Glu Asp Gln Ala Pro Thr Met Glu
 595 600

<210> 76

<211> 2022

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 76

Met Ser Val Lys Glu Ala Gly Ser Ser Gly Arg Arg Glu Gln Ala Ala
 1 5 10 15

Tyr His Leu His Ile Tyr Pro Gln Leu Ser Thr Thr Glu Ser Gln Ala
 20 25 30

Ser Cys Arg Val Thr Ala Thr Lys Asp Ser Thr Thr Ser Asp Val Ile
 35 40 45

Lys Asp Ala Ile Ala Ser Leu Arg Leu Asp Gly Thr Lys Cys Tyr Val
 50 55 60

Leu Val Glu Val Lys Glu Ser Gly Gly Glu Glu Trp Val Leu Asp Ala
 65 70 75 80

Asn Asp Ser Pro Val His Arg Val Leu Leu Trp Pro Arg Arg Ala Gln
 85 90 95

Asp Glu His Pro Gln Glu Asp Gly Tyr Tyr Phe Leu Leu Gln Glu Arg
 100 105 110

Asn Ala Asp Gly Thr Ile Lys Tyr Val His Met Gln Leu Val Ala Gln
 115 120 125

Ala Thr Ala Thr Arg Arg Leu Val Glu Arg Gly Leu Leu Pro Arg Gln
 130 135 140

Gln Ala Asp Phe Asp Asp Leu Cys Asn Leu Pro Glu Leu Thr Glu Gly
 145 150 155 160

Asn Leu Leu Lys Asn Leu Lys His Arg Phe Leu Gln Gln Lys Ile Tyr
 165 170 175

Thr Tyr Ala Gly Ser Ile Leu Val Ala Ile Asn Pro Phe Lys Phe Leu
 180 185 190

Pro Ile Tyr Asn Pro Lys Tyr Val Lys Met Tyr Glu Asn Gln Gln Leu
 195 200 205

Gly Lys Leu Glu Pro His Val Phe Ala Leu Ala Asp Val Ala Tyr Tyr
 210 215 220

Thr Met Leu Arg Lys Arg Val Asn Gln Cys Ile Val Tyr Pro Gly Glu
 225 230 235 240

Ser Gly Ser Gly Lys Thr Gln Ser Thr Asn Phe Leu Ile His Cys Leu
 245 250 255

Protein Complexes associated with APP-processing
 Thr Ala Leu Ser Gln Lys Gly Tyr Ala Ser Gly Val Glu Arg Thr Ile
 260 265 270

Leu Gly Ala Cys Pro Val Leu Glu Ala Phe Gly Asn Ala Lys Thr Ala
 275 280 285

His Asn Asn Asn Ser Ser Arg Phe Gly Lys Phe Ile Gln Val Ser Tyr
 290 295 300

Leu Glu Ser Gly Ile Val Arg Gly Ala Val Val Glu Lys Tyr Leu Leu
 305 310 315 320

Glu Lys Ser Arg Leu Val Ser Gln Glu Lys Asp Glu Arg Asn Tyr His
 325 330 335

Val Phe Tyr Tyr Leu Leu Leu Gly Val Ser Glu Glu Glu Arg Gln Glu
 340 345 350

Phe Gln Leu Lys Gln Pro Glu Asp Tyr Phe Tyr Leu Asn Gln His Asn
 355 360 365

Leu Lys Ile Glu Asp Gly Glu Asp Leu Lys His Asp Phe Glu Arg Leu
 370 375 380

Lys Gln Ala Met Glu Met Val Gly Phe Leu Pro Ala Thr Lys Lys Gln
 385 390 395 400

Ile Phe Ala Val Leu Ser Ala Ile Leu Tyr Leu Gly Asn Val Thr Tyr
 405 410 415

Lys Lys Arg Ala Thr Gly Arg Glu Glu Gly Leu Glu Val Gly Pro Pro
 420 425 430

Glu Val Leu Asp Thr Leu Ser Gln Leu Leu Lys Val Lys Arg Glu Ile
 435 440 445

Leu Val Glu Val Leu Thr Lys Arg Lys Thr Val Thr Val Asn Asp Lys
 450 455 460

Leu Ile Leu Pro Tyr Ser Leu Ser Glu Ala Ile Thr Ala Arg Asp Ser
 465 470 475 480

Met Ala Lys Ser Leu Tyr Ser Ala Leu Phe Asp Trp Ile Val Leu Arg
 485 490 495

Ile Asn His Ala Leu Leu Asn Lys Lys Asp Val Glu Glu Ala Val Ser
 500 505 510

Cys Leu Ser Ile Gly Val Leu Asp Ile Phe Gly Phe Glu Asp Phe Glu
 515 520 525

Protein Complexes associated with APP-processing
 Arg Asn Ser Phe Glu Gln Phe Cys Ile Asn Tyr Ala Asn Glu Gln Leu
 530 535 540

Gln Tyr Tyr Phe Asn Gln His Ile Phe Lys Leu Glu Gln Glu Glu Tyr
 545 550 555 560

Gln Gly Glu Gly Ile Thr Trp His Asn Ile Gly Tyr Thr Asp Asn Val
 565 570 575

Gly Cys Ile His Leu Ile Ser Lys Lys Pro Thr Gly Leu Phe Tyr Leu
 580 585 590

Leu Asp Glu Glu Ser Asn Phe Pro His Ala Thr Ser Gln Thr Leu Leu
 595 600 605

Ala Lys Phe Lys Gln Gln His Glu Asp Asn Lys Tyr Phe Leu Gly Thr
 610 615 620

Pro Val Met Glu Pro Ala Phe Ile Ile Gln His Phe Ala Gly Lys Val
 625 630 635 640

Lys Tyr Gln Ile Lys Asp Phe Arg Glu Lys Asn Met Asp Tyr Met Arg
 645 650 655

Pro Asp Ile Val Ala Leu Leu Arg Gly Ser Asp Ser Ser Tyr Val Arg
 660 665 670

Glu Leu Ile Gly Met Asp Pro Val Ala Val Phe Arg Trp Ala Val Leu
 675 680 685

Arg Ala Ala Ile Arg Ala Met Ala Val Leu Arg Glu Ala Gly Arg Leu
 690 695 700

Arg Ala Glu Arg Ala Glu Lys Ala Ala Gly Met Ser Ser Pro Gly Ala
 705 710 715 720

Gln Ser His Pro Glu Glu Leu Pro Arg Gly Ala Ser Thr Pro Ser Glu
 725 730 735

Lys Leu Tyr Arg Asp Leu His Asn Gln Met Ile Lys Ser Ile Lys Gly
 740 745 750

Leu Pro Trp Gln Gly Glu Asp Pro Arg Ser Leu Leu Gln Ser Leu Ser
 755 760 765

Arg Leu Gln Lys Pro Arg Ala Phe Ile Leu Lys Ser Lys Gly Ile Lys
 770 775 780

Gln Lys Gln Ile Ile Pro Lys Asn Leu Leu Asp Ser Lys Ser Leu Lys
 785 790 795 800

Protein Complexes associated with APP-processing
 Leu Ile Ile Ser Met Thr Leu His Asp Arg Thr Thr Lys Ser Leu Leu
 805 810 815

His Leu His Lys Lys Lys Lys Pro Pro Ser Ile Ser Ala Gln Phe Gln
 820 825 830

Thr Ser Leu Asn Lys Leu Leu Glu Ala Leu Gly Lys Ala Glu Pro Phe
 835 840 845

Phe Ile Arg Cys Ile Arg Ser Asn Ala Glu Lys Lys Glu Leu Cys Phe
 850 855 860

Asp Asp Glu Leu Val Leu Gln Gln Leu Arg Tyr Thr Gly Met Leu Glu
 865 870 875 880

Thr Val Arg Ile Arg Arg Ser Gly Tyr Ser Ala Lys Tyr Thr Phe Gln
 885 890 895

Asp Phe Thr Glu Gln Phe Gln Val Leu Leu Pro Lys Asp Ala Gln Pro
 900 905 910

Cys Arg Glu Val Ile Ser Thr Leu Leu Glu Lys Met Lys Ile Asp Lys
 915 920 925

Arg Asn Tyr Gln Ile Gly Lys Thr Lys Val Phe Leu Lys Glu Thr Glu
 930 935 940

Arg Gln Ala Leu Gln Glu Thr Leu His Arg Glu Val Val Arg Lys Ile
 945 950 955 960

Leu Leu Leu Gln Ser Trp Phe Arg Met Val Leu Glu Arg Arg His Phe
 965 970 975

Leu Gln Met Lys Arg Ala Ala Val Thr Ile Gln Ala Cys Trp Arg Ser
 980 985 990

Tyr Arg Val Arg Arg Ala Leu Glu Arg Thr Gln Ala Ala Val Tyr Leu
 995 1000 1005

Gln Ala Ala Trp Arg Gly Tyr Trp Gln Arg Lys Leu Tyr Arg His
 1010 1015 1020

Gln Lys Gln Ser Ile Ile Arg Leu Gln Ser Leu Cys Arg Gly His
 1025 1030 1035

Leu Gln Arg Lys Ser Phe Ser Gln Met Ile Ser Glu Lys Gln Lys
 1040 1045 1050

Ala Glu Glu Lys Glu Arg Glu Ala Leu Glu Ala Ala Arg Ala Gly
 1055 1060 1065

Protein Complexes associated with APP-processing

Ala	Glu	Glu	Gly	Gly	Gln	Gly	Gln	Ala	Ala	Gly	Gly	Gln	Gln	Val
	1070					1075						1080		
Ala	Glu	Gln	Gly	Pro	Glu	Pro	Ala	Glu	Asp	Gly	Gly	His	Leu	Ala
	1085					1090					1095			
Ser	Glu	Pro	Glu	Val	Gln	Pro	Ser	Asp	Arg	Ser	Pro	Leu	Glu	His
	1100					1105					1110			
Ser	Ser	Pro	Glu	Lys	Glu	Ala	Pro	Ser	Pro	Glu	Lys	Thr	Leu	Pro
	1115					1120					1125			
Pro	Gln	Lys	Thr	Val	Ala	Ala	Glu	Ser	His	Glu	Lys	Val	Pro	Ser
	1130					1135					1140			
Ser	Arg	Glu	Lys	Arg	Glu	Ser	Arg	Arg	Gln	Arg	Gly	Leu	Glu	His
	1145					1150					1155			
Val	Lys	Phe	Gln	Asn	Lys	His	Ile	Gln	Ser	Cys	Lys	Glu	Glu	Ser
	1160					1165					1170			
Ala	Leu	Arg	Glu	Pro	Ser	Arg	Arg	Val	Thr	Gln	Glu	Gln	Gly	Val
	1175					1180					1185			
Ser	Leu	Leu	Glu	Asp	Lys	Lys	Glu	Ser	Arg	Glu	Asp	Glu	Thr	Leu
	1190					1195					1200			
Leu	Val	Val	Glu	Thr	Glu	Ala	Glu	Asn	Thr	Ser	Gln	Lys	Gln	Pro
	1205					1210					1215			
Thr	Glu	Gln	Pro	Gln	Ala	Met	Ala	Val	Gly	Lys	Val	Ser	Glu	Glu
	1220					1225					1230			
Thr	Glu	Lys	Thr	Leu	Pro	Ser	Gly	Ser	Pro	Arg	Pro	Gly	Gln	Leu
	1235					1240					1245			
Glu	Arg	Pro	Thr	Ser	Leu	Ala	Leu	Asp	Ser	Arg	Val	Ser	Pro	Pro
	1250					1255					1260			
Ala	Pro	Gly	Ser	Ala	Pro	Glu	Thr	Pro	Glu	Asp	Lys	Ser	Lys	Pro
	1265					1270					1275			
Cys	Gly	Ser	Pro	Arg	Val	Gln	Glu	Lys	Pro	Asp	Ser	Pro	Gly	Gly
	1280					1285					1290			
Ser	Thr	Gln	Ile	Gln	Arg	Tyr	Leu	Asp	Ala	Glu	Arg	Leu	Ala	Ser
	1295					1300					1305			
Ala	Val	Glu	Leu	Trp	Arg	Gly	Lys	Lys	Leu	Val	Ala	Ala	Ala	Ser
	1310					1315					1320			

Protein Complexes associated with APP-processing

Pro Ser Ala Met Leu Ser Gln Ser Leu Asp Leu Ser Asp Arg His
1325 1330 1335

Arg Ala Thr Gly Ala Ala Leu Thr Pro Thr Glu Glu Arg Arg Thr
1340 1350

Ser Phe Ser Thr Ser Asp Val Ser Lys Leu Leu Pro Ser Leu Ala
1355 1360 1365

Lys Ala Gln Pro Ala Ala Glu Thr Thr Asp Gly Glu Arg Ser Ala
1370 1375 1380

Lys Lys Pro Ala Val Gln Lys Lys Lys Pro Gly Asp Ala Ser Ser
1385 1390 1395

Leu Pro Asp Ala Gly Leu Ser Pro Gly Ser Gln Val Asp Ser Lys
1400 1405 1410

Ser Thr Phe Lys Arg Leu Phe Leu His Lys Thr Lys Asp Lys Lys
1415 1420 1425

Tyr Ser Leu Glu Gly Ala Glu Glu Leu Glu Asn Ala Val Ser Gly
1430 1435 1440

His Val Val Leu Glu Ala Thr Thr Met Lys Lys Gly Leu Glu Ala
1445 1450 1455

Pro Ser Gly Gln Gln His Arg His Ala Ala Gly Glu Lys Arg Thr
1460 1465 1470

Lys Glu Pro Gly Gly Lys Gly Lys Lys Asn Arg Asn Val Lys Ile
1475 1480 1485

Gly Lys Ile Thr Val Ser Glu Lys Trp Arg Glu Ser Val Phe Arg
1490 1495 1500

Gln Ile Thr Asn Ala Asn Glu Leu Lys Tyr Leu Asp Glu Phe Leu
1505 1510 1515

Leu Asn Lys Ile Asn Asp Leu Arg Ser Gln Lys Thr Pro Ile Glu
1520 1525 1530

Ser Leu Phe Ile Glu Ala Thr Glu Lys Phe Arg Ser Asn Ile Lys
1535 1540 1545

Thr Met Tyr Ser Val Pro Asn Gly Lys Ile His Val Gly Tyr Lys
1550 1555 1560

Asp Leu Met Glu Asn Tyr Gln Ile Val Val Ser Asn Leu Ala Thr
1565 1570 1575

Protein Complexes associated with APP-processing

Glu	Arg	Gly	Gln	Lys	Asp	Thr	Asn	Leu	Val	Leu	Asn	Leu	Phe	Gln
	1580					1585					1590			
Ser	Leu	Leu	Asp	Glu	Phe	Thr	Arg	Gly	Tyr	Thr	Lys	Asn	Asp	Phe
	1595					1600					1605			
Glu	Pro	Val	Lys	Gln	Ser	Lys	Ala	Gln	Lys	Lys	Lys	Arg	Lys	Gln
	1610					1615					1620			
Glu	Arg	Ala	Val	Gln	Glu	His	Asn	Gly	His	Val	Phe	Ala	Ser	Tyr
	1625					1630					1635			
Gln	Val	Ser	Ile	Pro	Gln	Ser	Cys	Glu	Gln	Cys	Leu	Ser	Tyr	Ile
	1640					1645					1650			
Trp	Leu	Met	Asp	Lys	Ala	Leu	Leu	Cys	Ser	Val	Cys	Lys	Met	Thr
	1655					1660					1665			
Cys	His	Lys	Lys	Cys	Val	His	Lys	Ile	Gln	Ser	His	Cys	Ser	Tyr
	1670					1675					1680			
Thr	Tyr	Gly	Arg	Lys	Gly	Glu	Pro	Gly	Ala	Glu	Pro	Gly	His	Phe
	1685					1690					1695			
Gly	Val	Cys	Val	Asp	Ser	Leu	Thr	Ser	Asp	Lys	Ala	Ser	Val	Pro
	1700					1705					1710			
Ile	Val	Leu	Glu	Lys	Leu	Leu	Glu	His	Val	Glu	Met	His	Gly	Leu
	1715					1720					1725			
Tyr	Thr	Glu	Gly	Leu	Tyr	Arg	Lys	Ser	Gly	Ala	Ala	Asn	Arg	Thr
	1730					1735					1740			
Arg	Glu	Leu	Arg	Gln	Ala	Leu	Gln	Thr	Asp	Pro	Ala	Ala	Val	Lys
	1745					1750					1755			
Leu	Glu	Asn	Phe	Pro	Ile	His	Ala	Ile	Thr	Gly	Val	Leu	Lys	Gln
	1760					1765					1770			
Trp	Leu	Arg	Glu	Leu	Pro	Glu	Pro	Leu	Met	Thr	Phe	Ala	Gln	Tyr
	1775					1780					1785			
Gly	Asp	Phe	Leu	Arg	Ala	Val	Glu	Leu	Pro	Glu	Lys	Gln	Glu	Gln
	1790					1795					1800			
Leu	Ala	Ala	Ile	Tyr	Ala	Val	Leu	Glu	His	Leu	Pro	Glu	Ala	Asn
	1805					1810					1815			
His	Asn	Ser	Leu	Glu	Arg	Leu	Ile	Phe	His	Leu	Val	Lys	Val	Ala
	1820					1825					1830			

Protein Complexes associated with APP-processing

Leu Leu Glu Asp Val Asn Arg Met Ser Pro Gly Ala Leu Ala Ile
 1835 1840 1845
 Ile Phe Ala Pro Cys Leu Leu Arg Cys Pro Asp Asn Ser Asp Pro
 1850 1855 1860
 Leu Thr Ser Met Lys Asp Val Leu Lys Ile Thr Thr Cys Val Glu
 1865 1870 1875
 Met Leu Ile Lys Glu Gln Met Arg Lys Tyr Lys Val Lys Met Glu
 1880 1885 1890
 Glu Ile Ser Gln Leu Glu Ala Ala Glu Ser Ile Ala Phe Arg Arg
 1895 1900 1905
 Leu Ser Leu Leu Arg Gln Asn Ala Asn Lys Ser Pro Lys Thr Arg
 1910 1915 1920
 Glu Pro Ala Gly Gly Ala Gly Arg Leu Leu Thr Thr Ser Arg Val
 1925 1930 1935
 Ser Pro Ser Pro Ser Thr Arg Asn Leu Ala Leu Gly Ser Trp Arg
 1940 1945 1950
 Ser Ala Ala Leu Arg Thr Arg Gly Thr Gly Arg Pro Ala Arg Pro
 1955 1960 1965
 Gly Arg Ala Arg Ala Leu Arg Arg Arg Pro Pro Arg Pro Ala Arg
 1970 1975 1980
 Glu Ser Pro Ala Gln Pro Pro Arg Ser Arg Pro Arg Val Arg Thr
 1985 1990 1995
 Glu Thr Pro Ser Pro Leu Ser Ser Gly Pro Pro Pro Ser Arg Ser
 2000 2005 2010
 Asn Thr Gly Met Ala Pro Leu Arg Arg
 2015 2020

<210> 77

<211> 284

<212> PRT

<213> Homo sapiens

<400> 77

Met Ala Pro Arg Leu Cys Ser Ile Ser Val Thr Ala Arg Arg Leu Leu
 1 5 10 15

Protein Complexes associated with APP-processing

Gly Gly Pro Gly Pro Arg Ala Gly Asp Val Ala Ser Ala Ala Ala Ala
 20 25 30

Arg Phe Tyr Ser Lys Asp Asn Glu Gly Ser Trp Phe Arg Ser Leu Phe
 35 40 45

Val His Lys Val Asp Pro Arg Lys Asp Ala His Ser Thr Leu Leu Ser
 50 55 60

Lys Lys Glu Thr Ser Asn Leu Tyr Lys Ile Gln Phe His Asn Val Lys
 65 70 75 80

Pro Glu Tyr Leu Asp Ala Tyr Asn Ser Leu Thr Glu Ala Val Leu Pro
 85 90 95

Lys Leu His Leu Asp Glu Asp Tyr Pro Cys Ser Leu Val Gly Asn Trp
 100 105 110

Asn Thr Trp Tyr Gly Glu Gln Asp Gln Ala Val His Leu Trp Arg Phe
 115 120 125

Ser Gly Gly Tyr Pro Ala Leu Met Asp Cys Met Asn Lys Leu Lys Asn
 130 135 140

Asn Lys Glu Tyr Leu Glu Phe Arg Arg Glu Arg Ser Gln Met Leu Leu
 145 150 155 160

Ser Arg Arg Asn Gln Leu Leu Leu Glu Phe Ser Phe Trp Asn Glu Pro
 165 170 175

Gln Pro Arg Met Gly Pro Asn Ile Tyr Glu Leu Arg Thr Tyr Lys Leu
 180 185 190

Lys Pro Gly Thr Met Ile Glu Trp Gly Asn Asn Trp Ala Arg Ala Ile
 195 200 205

Lys Tyr Arg Gln Glu Asn Gln Glu Ala Val Gly Gly Phe Phe Ser Gln
 210 215 220

Ile Gly Glu Leu Tyr Val Val His His Leu Trp Ala Tyr Lys Asp Leu
 225 230 235 240

Gln Ser Arg Glu Glu Thr Arg Asn Ala Ala Trp Arg Lys Arg Gly Trp
 245 250 255

Asp Glu Asn Val Tyr Tyr Thr Val Pro Leu Val Arg His Met Glu Ser
 260 265 270

Arg Ile Met Ile Pro Leu Lys Ile Ser Pro Leu Gln
 275 280

Protein Complexes associated with APP-processing

<210> 78

<211> 286

<212> PRT

<213> Homo sapiens

<400> 78

Met Ala Ala Arg Val Leu Arg Ala Arg Gly Ala Ala Trp Ala Gly Gly
 1 5 10 15

Leu Leu Gln Arg Ala Ala Pro Cys Ser Leu Leu Pro Arg Leu Arg Thr
 20 25 30

Trp Thr Ser Ser Ser Asn Arg Ser Arg Glu Asp Ser Trp Leu Lys Ser
 35 40 45

Leu Phe Val Arg Lys Val Asp Pro Arg Lys Asp Ala His Ser Asn Leu
 50 55 60

Leu Ala Lys Lys Glu Thr Ser Asn Leu Tyr Lys Leu Gln Phe His Asn
 65 70 75 80

Val Lys Pro Glu Cys Leu Glu Ala Tyr Asn Lys Ile Cys Gln Glu Val
 85 90 95

Leu Pro Lys Ile His Glu Asp Lys His Tyr Pro Cys Thr Leu Val Gly
 100 105 110

Thr Trp Asn Thr Trp Tyr Gly Glu Gln Asp Gln Ala Val His Leu Trp
 115 120 125

Arg Tyr Glu Gly Gly Tyr Pro Ala Leu Thr Glu Val Met Asn Lys Leu
 130 135 140

Arg Glu Asn Lys Glu Phe Leu Glu Phe Arg Lys Ala Arg Ser Asp Met
 145 150 155 160

Leu Leu Ser Arg Lys Asn Gln Leu Leu Leu Glu Phe Ser Phe Trp Asn
 165 170 175

Glu Pro Val Pro Arg Ser Gly Pro Asn Ile Tyr Glu Leu Arg Ser Tyr
 180 185 190

Gln Leu Arg Pro Gly Thr Met Ile Glu Trp Gly Asn Tyr Trp Ala Arg
 195 200 205

Ala Ile Arg Phe Arg Gln Asp Gly Asn Glu Ala Val Gly Gly Phe Phe
 210 215 220

Protein Complexes associated with APP-processing
 Ser Gln Ile Gly Gln Leu Tyr Met Val His His Leu Trp Ala Tyr Arg
 225 230 235 240

Asp Leu Gln Thr Arg Glu Asp Ile Arg Asn Ala Ala Trp His Lys His
 245 250 255

Gly Trp Glu Glu Leu Val Tyr Tyr Thr Val Pro Leu Ile Gln Glu Met
 260 265 270

Glu Ser Arg Ile Met Ile Pro Leu Lys Thr Ser Pro Leu Gln
 275 280 285

<210> 79

<211> 1477

<212> PRT

<213> Homo sapiens

<400> 79

Met Gly Thr Ala Leu Leu Gln Arg Gly Gly Cys Phe Leu Leu Cys Leu
 1 5 10 15

Ser Leu Leu Leu Leu Gly Cys Trp Ala Glu Leu Gly Ser Gly Leu Glu
 20 25 30

Phe Pro Gly Ala Glu Gly Gln Trp Thr Arg Phe Pro Lys Trp Asn Ala
 35 40 45

Cys Cys Glu Ser Glu Met Ser Phe Gln Leu Lys Thr Arg Ser Ala Arg
 50 55 60

Gly Leu Val Leu Tyr Phe Asp Asp Glu Gly Phe Cys Asp Phe Leu Glu
 65 70 75 80

Leu Ile Leu Thr Arg Gly Gly Arg Leu Gln Leu Ser Phe Ser Ile Phe
 85 90 95

Cys Ala Glu Pro Ala Thr Leu Leu Ala Asp Thr Pro Val Asn Asp Gly
 100 105 110

Ala Trp His Ser Val Arg Ile Arg Arg Gln Phe Arg Asn Thr Thr Leu
 115 120 125

Phe Ile Asp Gln Val Glu Ala Lys Trp Val Glu Val Lys Ser Lys Arg
 130 135 140

Arg Asp Met Thr Val Phe Ser Gly Leu Phe Val Gly Gly Leu Pro Pro
 145 150 155 160

Protein Complexes associated with APP-processing

Glu Leu Arg Ala Ala Ala Leu Lys Leu Thr Leu Ala Ser Val Arg Glu
165 170 175

Arg Glu Pro Phe Lys Gly Trp Ile Arg Asp Val Arg Val Asn Ser Ser
180 185 190

Gln Val Leu Pro Val Asp Ser Gly Glu Val Lys Leu Asp Asp Glu Pro
195 200 205

Pro Asn Ser Gly Gly Gly Ser Pro Cys Glu Ala Gly Glu Glu Gly Glu
210 215 220

Gly Gly Val Cys Leu Asn Gly Gly Val Cys Ser Val Val Asp Asp Gln
225 230 235 240

Ala Val Cys Asp Cys Ser Arg Thr Gly Phe Arg Gly Lys Asp Cys Ser
245 250 255

Gln Glu Asp Asn Asn Val Glu Gly Leu Ala His Leu Met Met Gly Asp
260 265 270

Gln Gly Lys Ser Lys Gly Lys Glu Glu Tyr Ile Ala Thr Phe Lys Gly
275 280 285

Ser Glu Tyr Phe Cys Tyr Asp Leu Ser Gln Asn Pro Ile Gln Ser Ser
290 295 300

Ser Asp Glu Ile Thr Leu Ser Phe Lys Thr Leu Gln Arg Asn Gly Leu
305 310 315 320

Met Leu His Thr Gly Lys Ser Ala Asp Tyr Val Asn Leu Ala Leu Lys
325 330 335

Asn Gly Ala Val Ser Leu Val Ile Asn Leu Gly Ser Gly Ala Phe Glu
340 345 350

Ala Leu Val Glu Pro Val Asn Gly Lys Phe Asn Asp Asn Ala Trp His
355 360 365

Asp Val Lys Val Thr Arg Asn Leu Arg Gln His Ser Gly Ile Gly His
370 375 380

Ala Met Val Thr Ile Ser Val Asp Gly Ile Leu Thr Thr Thr Gly Tyr
385 390 395 400

Thr Gln Glu Asp Tyr Thr Met Leu Gly Ser Asp Asp Phe Phe Tyr Val
405 410 415

Gly Gly Ser Pro Ser Thr Ala Asp Leu Pro Gly Ser Pro Val Ser Asn
420 425 430

Protein Complexes associated with APP-processing

Asn Phe Met Gly Cys Leu Lys Glu Val Val Tyr Lys Asn Asn Asp Val
435 440 445

Arg Leu Glu Leu Ser Arg Leu Ala Lys Gln Gly Asp Pro Lys Met Lys
450 455 460

Ile His Gly Val Val Ala Phe Lys Cys Glu Asn Val Ala Thr Leu Asp
465 470 475 480

Pro Ile Thr Phe Glu Thr Pro Glu Ser Phe Ile Ser Leu Pro Lys Trp
485 490 495

Asn Ala Lys Lys Thr Gly Ser Ile Ser Phe Asp Phe Arg Thr Thr Glu
500 505 510

Pro Asn Gly Leu Ile Leu Phe Ser His Gly Lys Pro Arg His Gln Lys
515 520 525

Asp Ala Lys His Pro Gln Met Ile Lys Val Asp Phe Phe Ala Ile Glu
530 535 540

Met Leu Asp Gly His Leu Tyr Leu Leu Leu Asp Met Gly Ser Gly Thr
545 550 555 560

Ile Lys Ile Lys Ala Leu Leu Lys Lys Val Asn Asp Gly Glu Trp Tyr
565 570 575

His Val Asp Phe Gln Arg Asp Gly Arg Ser Gly Thr Ile Ser Val Asn
580 585 590

Thr Leu Arg Thr Pro Tyr Thr Ala Pro Gly Glu Ser Glu Ile Leu Asp
595 600 605

Leu Asp Asp Glu Leu Tyr Leu Gly Gly Leu Pro Glu Asn Lys Ala Gly
610 615 620

Leu Val Phe Pro Thr Glu Val Trp Thr Ala Leu Leu Asn Tyr Gly Tyr
625 630 635 640

Val Gly Cys Ile Arg Asp Leu Phe Ile Asp Gly Gln Ser Lys Asp Ile
645 650 655

Arg Gln Met Ala Glu Val Gln Ser Thr Ala Gly Val Lys Pro Ser Cys
660 665 670

Ser Lys Glu Thr Ala Lys Pro Cys Leu Ser Asn Pro Cys Lys Asn Asn
675 680 685

Gly Met Cys Arg Asp Gly Trp Asn Arg Tyr Val Cys Asp Cys Ser Gly
690 695 700

Protein Complexes associated with APP-processing

Thr Gly Tyr Leu Gly Arg Ser Cys Glu Arg Glu Ala Thr Val Leu Ser
 705 710 715 720
 Tyr Asp Gly Ser Met Phe Met Lys Ile Gln Leu Pro Val Val Met His
 725 730 735
 Thr Glu Ala Glu Asp Val Ser Leu Arg Phe Arg Ser Gln Arg Ala Tyr
 740 745 750
 Gly Ile Leu Met Ala Thr Thr Ser Arg Asp Ser Ala Asp Thr Leu Arg
 755 760 765
 Leu Glu Leu Asp Ala Gly Arg Val Lys Leu Thr Val Asn Leu Asp Cys
 770 775 780
 Ile Arg Ile Asn Cys Asn Ser Ser Lys Gly Pro Glu Thr Leu Phe Ala
 785 790 795 800
 Gly Tyr Asn Leu Asn Asp Asn Glu Trp His Thr Val Arg Val Val Arg
 805 810 815
 Arg Gly Lys Ser Leu Lys Leu Thr Val Asp Asp Gln Gln Ala Met Thr
 820 825 830
 Gly Gln Met Ala Gly Asp His Thr Arg Leu Glu Phe His Asn Ile Glu
 835 840 845
 Thr Gly Ile Ile Thr Glu Arg Arg Tyr Leu Ser Ser Val Pro Ser Asn
 850 855 860
 Phe Ile Gly His Leu Gln Ser Leu Thr Phe Asn Gly Met Ala Tyr Ile
 865 870 875 880
 Asp Leu Cys Lys Asn Gly Asp Ile Asp Tyr Cys Glu Leu Asn Ala Arg
 885 890 895
 Phe Gly Phe Arg Asn Ile Ile Ala Asp Pro Val Thr Phe Lys Thr Lys
 900 905 910
 Ser Ser Tyr Val Ala Leu Ala Thr Leu Gln Ala Tyr Thr Ser Met His
 915 920 925
 Leu Phe Phe Gln Phe Lys Thr Thr Ser Leu Asp Gly Leu Ile Leu Tyr
 930 935 940
 Asn Ser Gly Asp Gly Asn Asp Phe Ile Val Val Glu Leu Val Lys Gly
 945 950 955 960
 Tyr Leu His Tyr Val Phe Asp Leu Gly Asn Gly Ala Asn Leu Ile Lys
 965 970 975

Protein Complexes associated with APP-processing
 Gly Ser Ser Asn Lys Pro Leu Asn Asp Asn Gln Trp His Asn Val Met
 980 985 990

Ile Ser Arg Asp Thr Ser Asn Leu His Thr Val Lys Ile Asp Thr Lys
 995 1000 1005

Ile Thr Thr Gln Ile Thr Ala Gly Ala Arg Asn Leu Asp Leu Lys
 1010 1015 1020

Ser Asp Leu Tyr Ile Gly Gly Val Ala Lys Glu Thr Tyr Lys Ser
 1025 1030 1035

Leu Pro Lys Leu Val His Ala Lys Glu Gly Phe Gln Gly Cys Leu
 1040 1045 1050

Ala Ser Val Asp Leu Asn Gly Arg Leu Pro Asp Leu Ile Ser Asp
 1055 1060 1065

Ala Leu Phe Cys Asn Gly Gln Ile Glu Arg Gly Cys Glu Gly Pro
 1070 1075 1080

Ser Thr Thr Cys Gln Glu Asp Ser Cys Ser Asn Gln Gly Val Cys
 1085 1090 1095

Leu Gln Gln Trp Asp Gly Phe Ser Cys Asp Cys Ser Met Thr Ser
 1100 1105 1110

Phe Ser Gly Pro Leu Cys Asn Asp Pro Gly Thr Thr Tyr Ile Phe
 1115 1120 1125

Ser Lys Gly Gly Gly Gln Ile Thr Tyr Lys Trp Pro Pro Asn Asp
 1130 1135 1140

Arg Pro Ser Thr Arg Ala Asp Arg Leu Ala Ile Gly Phe Ser Thr
 1145 1150 1155

Val Gln Lys Glu Ala Val Leu Val Arg Val Asp Ser Ser Ser Gly
 1160 1165 1170

Leu Gly Asp Tyr Leu Glu Leu His Ile His Gln Gly Lys Ile Gly
 1175 1180 1185

Val Lys Phe Asn Val Gly Thr Asp Asp Ile Ala Ile Glu Glu Ser
 1190 1195 1200

Asn Ala Ile Ile Asn Asp Gly Lys Tyr His Val Val Arg Phe Thr
 1205 1210 1215

Arg Ser Gly Gly Asn Ala Thr Leu Gln Val Asp Ser Trp Pro Val
 1220 1225 1230

Protein Complexes associated with APP-processing

Ile	Glu	Arg	Tyr	Pro	Ala	Gly	Arg	Gln	Leu	Thr	Ile	Phe	Asn	Ser
1235						1240					1245			
Gln	Ala	Thr	Ile	Ile	Ile	Gly	Gly	Lys	Glu	Gln	Gly	Gln	Pro	Phe
1250						1255					1260			
Gln	Gly	Gln	Leu	Ser	Gly	Leu	Tyr	Tyr	Asn	Gly	Leu	Lys	Val	Leu
1265						1270					1275			
Asn	Met	Ala	Ala	Glu	Asn	Asp	Ala	Asn	Ile	Ala	Ile	Val	Gly	Asn
1280						1285					1290			
Val	Arg	Leu	Val	Gly	Glu	Val	Pro	Ser	Ser	Met	Thr	Thr	Glu	Ser
1295						1300					1305			
Thr	Ala	Thr	Ala	Met	Gln	Ser	Glu	Met	Ser	Thr	Ser	Ile	Met	Glu
1310						1315					1320			
Thr	Thr	Thr	Thr	Leu	Ala	Thr	Ser	Thr	Ala	Arg	Arg	Gly	Lys	Pro
1325						1330					1335			
Pro	Thr	Lys	Glu	Pro	Ile	Ser	Gln	Thr	Thr	Asp	Asp	Ile	Leu	Val
1340						1345					1350			
Ala	Ser	Ala	Glu	Cys	Pro	Ser	Asp	Asp	Glu	Asp	Ile	Asp	Pro	Cys
1355						1360					1365			
Glu	Pro	Ser	Ser	Gly	Gly	Leu	Ala	Asn	Pro	Thr	Arg	Ala	Gly	Gly
1370						1375					1380			
Arg	Glu	Pro	Tyr	Pro	Gly	Ser	Ala	Glu	Val	Ile	Arg	Glu	Ser	Ser
1385						1390					1395			
Ser	Thr	Thr	Gly	Met	Val	Val	Gly	Ile	Val	Ala	Ala	Ala	Ala	Leu
1400						1405					1410			
Cys	Ile	Leu	Ile	Leu	Leu	Tyr	Ala	Met	Tyr	Lys	Tyr	Arg	Asn	Arg
1415						1420					1425			
Asp	Glu	Gly	Ser	Tyr	His	Val	Asp	Glu	Ser	Arg	Asn	Tyr	Ile	Ser
1430						1435					1440			
Asn	Ser	Ala	Gln	Ser	Asn	Gly	Ala	Val	Val	Lys	Glu	Lys	Gln	Pro
1445						1450					1455			
Ser	Ser	Ala	Lys	Ser	Ser	Asn	Lys	Asn	Lys	Lys	Asn	Lys	Asp	Lys
1460						1465					1470			
Glu	Tyr	Tyr	Val											
1475														

Protein Complexes associated with APP-processing

<210> 80

<211> 329

<212> PRT

<213> Homo sapiens

<400> 80

Met Thr Thr Gln Gln Ile Asp Leu Gln Gly Pro Gly Pro Trp Gly Phe
 1 5 10 15

Arg Leu Val Gly Gly Lys Asp Phe Glu Gln Pro Leu Ala Ile Ser Arg
 20 25 30

Val Thr Pro Gly Ser Lys Ala Ala Leu Ala Asn Leu Cys Ile Gly Asp
 35 40 45

Val Ile Thr Ala Ile Asp Gly Glu Asn Thr Ser Asn Met Thr His Leu
 50 55 60

Glu Ala Gln Asn Arg Ile Lys Gly Cys Thr Asp Asn Leu Thr Leu Thr
 65 70 75 80

Val Ala Arg Ser Glu His Lys Val Trp Ser Pro Leu Val Thr Glu Glu
 85 90 95

Gly Lys Arg His Pro Tyr Lys Met Asn Leu Ala Ser Glu Pro Gln Glu
 100 105 110

Val Leu His Ile Gly Ser Ala His Asn Arg Ser Ala Met Pro Phe Thr
 115 120 125

Ala Ser Pro Ala Ser Ser Thr Thr Ala Arg Val Ile Thr Asn Gln Tyr
 130 135 140

Asn Asn Pro Ala Gly Leu Tyr Ser Ser Glu Asn Ile Ser Asn Phe Asn
 145 150 155 160

Asn Ala Leu Glu Ser Lys Thr Ala Ala Ser Gly Val Glu Ala Asn Ser
 165 170 175

Arg Pro Leu Asp His Ala Gln Pro Pro Ser Ser Leu Val Ile Asp Lys
 180 185 190

Glu Ser Glu Val Tyr Lys Met Leu Gln Glu Lys Gln Glu Leu Asn Glu
 195 200 205

Pro Pro Lys Gln Ser Thr Ser Phe Leu Val Leu Gln Glu Ile Leu Glu
 210 215 220

Protein Complexes associated with APP-processing

Ser Glu Glu Lys Gly Asp Pro Asn Lys Pro Ser Gly Phe Arg Ser Val
 225 230 235 240

Lys Ala Pro Val Thr Lys Val Ala Ala Ser Ile Gly Asn Ala Gln Lys
 245 250 255

Leu Pro Met Cys Asp Lys Cys Gly Thr Gly Ile Val Gly Val Phe Val
 260 265 270

Lys Leu Arg Asp Arg His Arg His Pro Glu Cys Tyr Val Cys Thr Asp
 275 280 285

Cys Gly Thr Asn Leu Lys Gln Lys Gly His Phe Phe Val Glu Asp Gln
 290 295 300

Ile Tyr Cys Glu Lys His Ala Arg Glu Arg Val Thr Pro Pro Glu Gly
 305 310 315 320

Tyr Glu Val Val Thr Val Phe Pro Lys
 325

<210> 81

<211> 547

<212> PRT

<213> Homo sapiens

<400> 81

Met Thr Ser Ala Ala Pro Ala Lys Lys Pro Tyr Arg Lys Ala Pro Pro
 1 5 10 15

Glu His Arg Glu Leu Arg Leu Glu Ile Pro Gly Ser Arg Leu Glu Gln
 20 25 30

Glu Glu Pro Leu Thr Asp Ala Glu Arg Met Lys Leu Leu Gln Glu Glu
 35 40 45

Asn Glu Glu Leu Arg Arg Arg Leu Ala Ser Ala Thr Arg Arg Thr Glu
 50 55 60

Ala Leu Glu Arg Glu Leu Glu Ile Gly Gln Asp Cys Leu Glu Leu Glu
 65 70 75 80

Leu Gly Gln Ser Arg Glu Glu Leu Asp Lys Phe Lys Asp Lys Phe Arg
 85 90 95

Arg Leu Gln Asn Ser Tyr Thr Ala Ser Gln Arg Thr Asn Gln Glu Leu
 100 105 110

Protein Complexes associated with APP-processing

Glu Asp Lys Leu His Thr Leu Ile Lys Lys Ala Glu Met Asp Arg Lys
 115 120 125

Thr Leu Asp Trp Glu Ile Val Glu Leu Thr Asn Lys Leu Leu Asp Ala
 130 135 140

Lys Asn Thr Ile Asn Lys Leu Glu Glu Leu Asn Glu Arg Tyr Arg Leu
 145 150 155 160

Asp Cys Asn Pro Ala Val Gln Leu Leu Lys Cys Asn Lys Ser His Phe
 165 170 175

Arg Asn His Lys Phe Ala Asp Leu Pro Cys Glu Leu Gln Asp Met Val
 180 185 190

Arg Lys His Leu His Ser Gly Gln Glu Ala Ala Ser Pro Gly Pro Ala
 195 200 205

Pro Ser Leu Ala Pro Gly Ala Val Val Pro Thr Ser Val Ile Ala Arg
 210 215 220

Val Leu Glu Lys Pro Glu Ser Leu Leu Leu Asn Ser Ala Gln Ser Gly
 225 230 235 240

Ser Ala Gly Arg Pro Leu Ala Glu Asp Val Phe Val His Val Asp Met
 245 250 255

Ser Glu Gly Val Pro Gly Asp Pro Ala Ser Pro Pro Ala Pro Gly Ser
 260 265 270

Pro Thr Pro Gln Pro Asn Gly Glu Cys His Ser Leu Gly Thr Ala Arg
 275 280 285

Gly Ser Pro Glu Glu Glu Leu Pro Leu Pro Ala Phe Glu Lys Leu Asn
 290 295 300

Pro Tyr Pro Thr Pro Ser Pro Pro His Pro Leu Tyr Pro Gly Arg Arg
 305 310 315 320

Val Ile Glu Phe Ser Glu Asp Lys Val Arg Ile Pro Arg Asn Ser Pro
 325 330 335

Leu Pro Asn Cys Thr Tyr Ala Thr Arg Gln Ala Ile Ser Leu Ser Leu
 340 345 350

Val Glu Glu Gly Ser Glu Arg Ala Arg Pro Ser Pro Val Pro Ser Thr
 355 360 365

Pro Ala Ser Ala Gln Ala Ser Pro His His Gln Pro Ser Pro Ala Pro
 370 375 380

Protein Complexes associated with APP-processing

Leu Thr Leu Ser Ala Pro Ala Ser Ser Ala Ser Ser Glu Glu Asp Leu
 385 390 395 400

Leu Val Ser Trp Gln Arg Ala Phe Val Asp Arg Thr Pro Pro Pro Ala
 405 410 415

Ala Val Ala Gln Arg Thr Ala Phe Gly Arg Asp Ala Leu Pro Glu Leu
 420 425 430

Gln Arg His Phe Ala His Ser Pro Ala Asp Arg Asp Glu Val Val Gln
 435 440 445

Ala Pro Ser Ala Arg Pro Glu Glu Ser Glu Leu Leu Leu Pro Thr Glu
 450 455 460

Pro Asp Ser Gly Phe Pro Arg Glu Glu Glu Glu Leu Asn Leu Pro Ile
 465 470 475 480

Ser Pro Glu Glu Glu Arg Gln Ser Leu Leu Pro Ile Asn Arg Gly Thr
 485 490 495

Glu Glu Gly Pro Gly Thr Ser His Thr Glu Gly Arg Ala Trp Pro Leu
 500 505 510

Pro Ser Ser Ser Arg Pro Gln Arg Ser Pro Lys Arg Met Gly Val His
 515 520 525

His Leu His Arg Lys Asp Ser Leu Thr Gln Ala Gln Glu Gln Gly Asn
 530 535 540

Leu Leu Asn
 545

<210> 82

<211> 856

<212> PRT

<213> Homo sapiens

<400> 82

Met Gly Thr Thr Ala Ser Thr Ala Gln Gln Thr Val Ser Ala Gly Thr
 1 5 10 15

Pro Phe Glu Gly Leu Gln Gly Ser Gly Thr Met Asp Ser Arg His Ser
 20 25 30

Val Ser Ile His Ser Phe Gln Ser Thr Ser Leu His Asn Ser Lys Ala
 35 40 45

Protein Complexes associated with APP-processing

Lys Ser Ile Ile Pro Asn Lys Val Ala Pro Val Val Ile Thr Tyr Asn
50 55 60

Cys Lys Glu Glu Phe Gln Ile His Asp Glu Leu Leu Lys Ala His Tyr
65 70 75 80

Thr Leu Gly Arg Leu Ser Asp Asn Thr Pro Glu His Tyr Leu Val Gln
85 90 95

Gly Arg Tyr Phe Leu Val Arg Asp Val Thr Glu Lys Met Asp Val Leu
100 105 110

Gly Thr Val Gly Ser Cys Gly Ala Pro Asn Phe Arg Gln Val Gln Gly
115 120 125

Gly Leu Thr Val Phe Gly Met Gly Gln Pro Ser Leu Ser Gly Phe Arg
130 135 140

Arg Val Leu Gln Lys Leu Gln Lys Asp Gly His Arg Glu Cys Val Ile
145 150 155 160

Phe Cys Val Arg Glu Glu Pro Val Leu Phe Leu Arg Ala Asp Glu Asp
165 170 175

Phe Val Ser Tyr Thr Pro Arg Asp Lys Gln Asn Leu His Glu Asn Leu
180 185 190

Gln Gly Leu Gly Pro Gly Val Arg Val Glu Ser Leu Glu Leu Ala Ile
195 200 205

Arg Lys Glu Ile His Asp Phe Ala Gln Leu Ser Glu Asn Thr Tyr His
210 215 220

Val Tyr His Asn Thr Glu Asp Leu Trp Gly Glu Pro His Ala Val Ala
225 230 235 240

Ile His Gly Glu Asp Asp Leu His Val Thr Glu Glu Val Tyr Lys Arg
245 250 255

Pro Leu Phe Leu Gln Pro Thr Tyr Arg Tyr His Arg Leu Pro Leu Pro
260 265 270

Glu Gln Gly Ser Pro Leu Glu Ala Gln Leu Asp Ala Phe Val Ser Val
275 280 285

Leu Arg Glu Thr Pro Ser Leu Leu Gln Leu Arg Asp Ala His Gly Pro
290 295 300

Pro Pro Ala Leu Val Phe Ser Cys Gln Met Gly Val Gly Arg Thr Asn
305 310 315 320

Protein Complexes associated with APP-processing

Leu Gly Met Val Leu Gly Thr Leu Ile Leu Leu His Arg Ser Gly Thr
 325 330 335

Thr Ser Gln Pro Glu Ala Ala Pro Thr Gln Ala Lys Pro Leu Pro Met
 340 345 350

Glu Gln Phe Gln Val Ile Gln Ser Phe Leu Arg Met Val Pro Gln Gly
 355 360 365

Arg Arg Met Val Glu Glu Val Asp Arg Ala Ile Thr Ala Cys Ala Glu
 370 375 380

Leu His Asp Leu Lys Glu Val Val Leu Glu Asn Gln Lys Lys Leu Glu
 385 390 395 400

Gly Ile Arg Pro Glu Ser Pro Ala Gln Gly Ser Gly Ser Arg His Ser
 405 410 415

Val Trp Gln Arg Ala Leu Trp Ser Leu Glu Arg Tyr Phe Tyr Leu Ile
 420 425 430

Leu Phe Asn Tyr Tyr Leu His Glu Gln Tyr Pro Leu Ala Phe Ala Leu
 435 440 445

Ser Phe Ser Arg Trp Leu Cys Ala His Pro Glu Leu Tyr Arg Leu Pro
 450 455 460

Val Thr Leu Ser Ser Ala Gly Pro Val Ala Pro Arg Asp Leu Ile Ala
 465 470 475 480

Arg Gly Ser Leu Arg Glu Asp Asp Leu Val Ser Pro Asp Ala Leu Ser
 485 490 495

Thr Val Arg Glu Met Asp Val Ala Asn Phe Arg Arg Val Pro Arg Met
 500 505 510

Pro Ile Tyr Gly Thr Ala Gln Pro Ser Ala Lys Ala Leu Gly Ser Ile
 515 520 525

Leu Ala Tyr Leu Thr Asp Ala Lys Arg Arg Leu Arg Lys Val Val Trp
 530 535 540

Val Ser Leu Arg Glu Glu Ala Val Leu Glu Cys Asp Gly His Thr Tyr
 545 550 555 560

Ser Leu Arg Trp Pro Gly Pro Pro Val Ala Pro Asp Gln Leu Glu Thr
 565 570 575

Leu Glu Ala Gln Leu Lys Ala His Leu Ser Glu Pro Pro Pro Gly Lys
 580 585 590

Protein Complexes associated with APP-processing

Glu Gly Pro Leu Thr Tyr Arg Phe Gln Thr Cys Leu Thr Met Gln Glu
 595 600 605

Val Phe Ser Gln His Arg Arg Ala Cys Pro Gly Leu Thr Tyr His Arg
 610 615 620

Ile Pro Met Pro Asp Phe Cys Ala Pro Arg Glu Glu Asp Phe Asp Gln
 625 630 635 640

Leu Leu Glu Ala Leu Arg Ala Ala Leu Ser Lys Asp Pro Gly Thr Gly
 645 650 655

Phe Val Phe Ser Cys Leu Ser Gly Gln Gly Arg Thr Thr Thr Ala Met
 660 665 670

Val Val Ala Val Leu Ala Phe Trp His Ile Gln Gly Phe Pro Glu Val
 675 680 685

Gly Glu Glu Glu Leu Val Ser Val Pro Asp Ala Lys Phe Thr Lys Gly
 690 695 700

Glu Phe Gln Val Val Met Lys Val Val Gln Leu Leu Pro Asp Gly His
 705 710 715 720

Arg Val Lys Lys Glu Val Asp Ala Ala Leu Asp Thr Val Ser Glu Thr
 725 730 735

Met Thr Pro Met His Tyr His Leu Arg Glu Ile Ile Ile Cys Thr Tyr
 740 745 750

Arg Gln Ala Lys Ala Ala Lys Glu Ala Gln Glu Met Arg Arg Leu Gln
 755 760 765

Leu Arg Ser Leu Gln Tyr Leu Glu Arg Tyr Val Cys Leu Ile Leu Phe
 770 775 780

Asn Ala Tyr Leu His Leu Glu Lys Ala Asp Ser Trp Gln Arg Pro Phe
 785 790 795 800

Ser Thr Trp Met Gln Glu Val Ala Ser Lys Ala Gly Ile Tyr Glu Ile
 805 810 815

Leu Asn Glu Leu Gly Phe Pro Glu Leu Glu Ser Gly Glu Asp Gln Pro
 820 825 830

Phe Ser Arg Leu Arg Tyr Arg Trp Gln Glu Gln Ser Cys Ser Leu Glu
 835 840 845

Pro Ser Ala Pro Glu Asp Leu Leu
 850 855

Protein Complexes associated with APP-processing

<210> 83

<211> 271

<212> PRT

<213> Homo sapiens

<400> 83

Met Glu Ala Leu Pro Leu Leu Ala Ala Thr Thr Pro Asp His Gly Arg
 1 5 10 15

His Arg Arg Leu Leu Leu Pro Leu Leu Leu Phe Leu Leu Pro Ala
 20 25 30

Gly Ala Val Gln Gly Trp Glu Thr Glu Glu Arg Pro Arg Thr Arg Glu
 35 40 45

Glu Glu Cys His Phe Tyr Ala Gly Gly Gln Val Tyr Pro Gly Glu Ala
 50 55 60

Ser Arg Val Ser Val Ala Asp His Ser Leu His Leu Ser Lys Ala Lys
 65 70 75 80

Ile Ser Lys Pro Ala Pro Tyr Trp Glu Gly Thr Ala Val Ile Asp Gly
 85 90 95

Glu Phe Lys Glu Leu Lys Leu Thr Asp Tyr Arg Gly Lys Tyr Leu Val
 100 105 110

Phe Phe Phe Tyr Pro Leu Asp Phe Thr Phe Val Cys Pro Thr Glu Ile
 115 120 125

Ile Ala Phe Gly Asp Arg Leu Glu Glu Phe Arg Ser Ile Asn Thr Glu
 130 135 140

Val Val Ala Cys Ser Val Asp Ser Gln Phe Thr His Leu Ala Trp Ile
 145 150 155 160

Asn Thr Pro Arg Arg Gln Gly Gly Leu Gly Pro Ile Arg Ile Pro Leu
 165 170 175

Leu Ser Asp Leu Thr His Gln Ile Ser Lys Asp Tyr Gly Val Tyr Leu
 180 185 190

Glu Asp Ser Gly His Thr Leu Arg Gly Leu Phe Ile Ile Asp Asp Lys
 195 200 205

Gly Ile Leu Arg Gln Ile Thr Leu Asn Asp Leu Pro Val Gly Arg Ser
 210 215 220

Protein Complexes associated with APP-processing
 Val Asp Glu Thr Leu Arg Leu Val Gln Ala Phe Gln Tyr Thr Asp Lys
 225 230 235 240

His Gly Glu Val Cys Pro Ala Gly Trp Lys Pro Gly Ser Glu Thr Ile
 245 250 255

Ile Pro Asp Pro Ala Gly Lys Leu Lys Tyr Phe Asp Lys Leu Asn
 260 265 270

<210> 84

<211> 640

<212> PRT

<213> Homo sapiens

<400> 84

Met Ala Ala Leu Tyr Arg Pro Gly Leu Arg Leu Asn Trp His Gly Leu
 1 5 10 15

Ser Pro Leu Gly Trp Pro Ser Cys Arg Ser Ile Gln Thr Leu Arg Val
 20 25 30

Leu Ser Gly Asp Leu Gly Gln Leu Pro Thr Gly Ile Arg Asp Phe Val
 35 40 45

Glu His Ser Ala Arg Leu Cys Gln Pro Glu Gly Ile His Ile Cys Asp
 50 55 60

Gly Thr Glu Ala Glu Asn Thr Ala Thr Leu Thr Leu Leu Glu Gln Gln
 65 70 75 80

Gly Leu Ile Arg Lys Leu Pro Lys Tyr Asn Asn Cys Trp Leu Ala Arg
 85 90 95

Thr Asp Pro Lys Asp Val Ala Arg Val Glu Ser Lys Thr Val Ile Val
 100 105 110

Thr Pro Ser Gln Arg Asp Thr Val Pro Leu Pro Pro Gly Gly Ala Arg
 115 120 125

Gly Gln Leu Gly Asn Trp Met Ser Pro Ala Asp Phe Gln Arg Ala Val
 130 135 140

Asp Glu Arg Phe Pro Gly Cys Met Gln Gly Arg Thr Met Tyr Val Leu
 145 150 155 160

Pro Phe Ser Met Gly Pro Val Gly Ser Pro Leu Ser Arg Ile Gly Val
 165 170 175

Protein Complexes associated with APP-processing

Gln Leu Thr Asp Ser Ala Tyr Val Val Ala Ser Met Arg Ile Met Thr
 180 185 190

Arg Leu Gly Thr Pro Val Leu Gln Ala Leu Gly Asp Gly Asp Phe Val
 195 200 205

Lys Cys Leu His Ser Val Gly Gln Pro Leu Thr Gly Gln Gly Glu Pro
 210 215 220

Val Ser Gln Trp Pro Cys Asn Pro Glu Lys Thr Leu Ile Gly His Val
 225 230 235 240

Pro Asp Gln Arg Glu Ile Ile Ser Phe Gly Ser Gly Tyr Gly Gly Asn
 245 250 255

Ser Leu Leu Gly Lys Lys Cys Phe Ala Leu Arg Ile Ala Ser Arg Leu
 260 265 270

Ala Arg Asp Glu Gly Trp Leu Ala Glu His Met Leu Ile Leu Gly Ile
 275 280 285

Thr Ser Pro Ala Gly Lys Lys Ala Leu Cys Ala Ala Ala Phe Pro Ser
 290 295 300

Ala Cys Gly Lys Thr Asn Leu Ala Met Met Arg Pro Ala Leu Pro Gly
 305 310 315 320

Trp Lys Val Glu Cys Val Gly Asp Asp Ile Ala Trp Met Arg Phe Asp
 325 330 335

Ser Glu Gly Arg Leu Arg Ala Ile Asn Pro Glu Asn Gly Phe Phe Gly
 340 345 350

Val Ala Pro Gly Thr Ser Ala Thr Thr Asn Pro Asn Ala Met Ala Thr
 355 360 365

Ile Gln Ser Asn Thr Ile Phe Thr Asn Val Ala Glu Thr Ser Asp Gly
 370 375 380

Gly Val Tyr Trp Glu Gly Ile Asp Gln Pro Leu Pro Pro Gly Val Thr
 385 390 395 400

Val Thr Ser Trp Leu Gly Lys Pro Trp Lys Pro Gly Asp Lys Glu Pro
 405 410 415

Cys Ala His Pro Asn Ser Arg Phe Cys Ala Pro Ala Arg Gln Cys Pro
 420 425 430

Ile Met Asp Pro Ala Trp Glu Ala Pro Glu Gly Val Pro Ile Asp Ala
 435 440 445

Protein Complexes associated with APP-processing

Ile Ile Phe Gly Gly Arg Arg Pro Lys Gly Val Pro Leu Val Tyr Glu
 450 455 460

Ala Phe Asn Trp Arg His Gly Val Phe Val Gly Arg Ala Met Arg Ser
 465 470 475 480

Glu Ser Thr Ala Ala Ala Glu His Lys Gly Lys Ile Ile Met His Asp
 485 490 495

Pro Phe Ala Met Arg Pro Phe Phe Gly Tyr Asn Phe Gly His Tyr Leu
 500 505 510

Glu His Trp Leu Ser Met Glu Gly Arg Lys Gly Ala Gln Leu Pro Arg
 515 520 525

Ile Phe His Val Asn Trp Phe Arg Arg Asp Glu Ala Gly His Phe Leu
 530 535 540

Trp Pro Gly Phe Gly Glu Asn Ala Arg Val Leu Asp Trp Ile Cys Arg
 545 550 555 560

Arg Leu Glu Gly Glu Asp Ser Ala Arg Glu Thr Pro Ile Gly Leu Val
 565 570 575

Pro Lys Glu Gly Ala Leu Asp Leu Ser Gly Leu Arg Ala Ile Asp Thr
 580 585 590

Thr Gln Leu Phe Ser Leu Pro Lys Asp Phe Trp Glu Gln Glu Val Arg
 595 600 605

Asp Ile Arg Ser Tyr Leu Thr Glu Gln Val Asn Gln Asp Leu Pro Lys
 610 615 620

Glu Val Leu Ala Glu Leu Glu Ala Leu Glu Arg Arg Val His Lys Met
 625 630 635 640

<210> 85

<211> 449

<212> PRT

<213> Homo sapiens

<400> 85

Met Leu Pro Ala Ala Thr Ala Ser Leu Leu Gly Pro Leu Leu Thr Ala
 1 5 10 15

Cys Ala Leu Leu Pro Phe Ala Gln Gly Gln Thr Pro Asn Tyr Thr Arg
 20 25 30

Protein Complexes associated with APP-processing

Pro Val Phe Leu Cys Gly Gly Asp Val Lys Gly Glu Ser Gly Tyr Val
 35 40 45

Ala Ser Glu Gly Phe Pro Asn Leu Tyr Pro Pro Asn Lys Glu Cys Ile
 50 55 60

Trp Thr Ile Thr Val Pro Glu Gly Gln Thr Val Ser Leu Ser Phe Arg
 65 70 75 80

Val Phe Asp Leu Glu Leu His Pro Ala Cys Arg Tyr Asp Ala Leu Glu
 85 90 95

Val Phe Ala Gly Ser Gly Thr Ser Gly Gln Arg Leu Gly Arg Phe Cys
 100 105 110

Gly Thr Phe Arg Pro Ala Pro Leu Val Ala Pro Gly Asn Gln Val Thr
 115 120 125

Leu Arg Met Thr Thr Asp Glu Gly Thr Gly Gly Arg Gly Phe Leu Leu
 130 135 140

Trp Tyr Ser Gly Arg Ala Thr Ser Gly Thr Glu His Gln Phe Cys Gly
 145 150 155 160

Gly Arg Leu Glu Lys Ala Gln Gly Thr Leu Thr Thr Pro Asn Trp Pro
 165 170 175

Glu Ser Asp Tyr Pro Pro Gly Ile Ser Cys Ser Trp His Ile Ile Ala
 180 185 190

Pro Pro Asp Gln Val Ile Ala Leu Thr Phe Glu Lys Phe Asp Leu Glu
 195 200 205

Pro Asp Thr Tyr Cys Arg Tyr Asp Ser Val Ser Val Phe Asn Gly Ala
 210 215 220

Val Ser Asp Asp Ser Arg Arg Leu Gly Lys Phe Cys Gly Asp Ala Val
 225 230 235 240

Pro Gly Ser Ile Ser Ser Glu Gly Asn Glu Leu Leu Val Gln Phe Val
 245 250 255

Ser Asp Leu Ser Val Thr Ala Asp Gly Phe Ser Ala Ser Tyr Lys Thr
 260 265 270

Leu Pro Arg Gly Thr Ala Lys Glu Gly Gln Gly Pro Gly Pro Lys Arg
 275 280 285

Gly Thr Glu Pro Lys Val Lys Leu Pro Pro Lys Ser Gln Pro Pro Glu
 290 295 300

Protein Complexes associated with APP-processing

Lys Thr Glu Glu Ser Pro Ser Ala Pro Asp Ala Pro Thr Cys Pro Lys
 305 310 315 320
 Gln Cys Arg Arg Thr Gly Thr Leu Gln Ser Asn Phe Cys Ala Ser Ser
 325 330 335
 Leu Val Val Thr Ala Thr Val Lys Ser Met Val Arg Glu Pro Gly Glu
 340 345 350
 Gly Leu Ala Val Thr Val Ser Leu Ile Gly Ala Tyr Lys Thr Gly Gly
 355 360 365
 Leu Asp Leu Pro Ser Pro Pro Thr Gly Ala Ser Leu Lys Phe Tyr Val
 370 375 380
 Pro Cys Lys Gln Cys Pro Pro Met Lys Lys Gly Val Ser Tyr Leu Leu
 385 390 395 400
 Met Gly Gln Val Glu Glu Asn Arg Gly Pro Val Leu Pro Pro Glu Ser
 405 410 415
 Phe Val Val Leu His Arg Pro Asn Gln Asp Gln Ile Leu Thr Asn Leu
 420 425 430
 Ser Lys Arg Lys Cys Pro Ser Gln Pro Val Arg Ala Ala Ala Ser Gln
 435 440 445

Asp

<210> 86

<211> 212

<212> PRT

<213> Homo sapiens

<400> 86

Met Arg Met Thr Met Glu Glu Met Lys Asn Glu Ala Glu Thr Thr Ser
 1 5 10 15
 Met Val Ser Met Pro Leu Tyr Ala Val Met Tyr Pro Val Phe Asn Glu
 20 25 30
 Leu Glu Arg Val Asn Leu Ser Ala Ala Gln Thr Leu Arg Ala Ala Phe
 35 40 45
 Ile Lys Ala Glu Lys Glu Asn Pro Gly Leu Thr Gln Asp Ile Ile Met
 50 55 60

Protein Complexes associated with APP-processing

Lys Ile Leu Glu Lys Lys Ser Val Glu Val Asn Phe Thr Glu Ser Leu
 65 70 75 80

Leu Arg Met Ala Ala Asp Asp Val Glu Glu Tyr Met Ile Glu Arg Pro
 85 90 95

Glu Pro Glu Phe Gln Ala Leu Asn Glu Lys Ala Arg Ala Leu Lys Gln
 100 105 110

Ile Leu Ser Lys Ile Pro Asp Glu Ile Asn Asp Arg Val Arg Phe Leu
 115 120 125

Gln Thr Ile Lys Asp Ile Ala Ser Ala Ile Lys Glu Leu Leu Asp Thr
 130 135 140

Val Asn Asn Val Phe Lys Lys Tyr Gln Tyr Gln Asn Arg Arg Ala Leu
 145 150 155 160

Glu His Gln Lys Lys Glu Phe Val Lys Tyr Ser Lys Ser Phe Ser Asp
 165 170 175

Thr Leu Lys Thr Tyr Phe Lys Asp Gly Lys Ala Ile Asn Val Phe Val
 180 185 190

Ser Ala Asn Arg Leu Ile His Gln Thr Asn Leu Ile Leu Gln Thr Phe
 195 200 205

Lys Thr Val Ala
 210

<210> 87

<211> 137

<212> PRT

<213> Homo sapiens.

<400> 87

Met Thr Ser Ala Leu Thr Gln Gly Leu Glu Arg Ile Pro Asp Gln Leu
 1 5 10 15

Gly Tyr Leu Val Leu Ser Glu Gly Ala Val Leu Ala Ser Ser Gly Asp
 20 25 30

Leu Glu Asn Asp Glu Gln Ala Ala Ser Ala Ile Ser Glu Leu Val Ser
 35 40 45

Thr Ala Cys Gly Phe Arg Leu His Arg Gly Met Asn Val Pro Phe Lys
 50 55 60

Protein Complexes associated with APP-processing
 Arg Leu Ser Gly Glu Pro Leu Pro Leu Pro Leu Val Val Val Leu Gly
 65 70 75 80

Ala Gly Gly Tyr Phe Gln Gly Leu Leu Gly Phe Ser Ser Ser Ser Leu
 85 90 95

Leu Pro Ser Pro Gly Val Ser Gly Leu Ala Thr Phe Leu Pro Leu Gly
 100 105 110

Leu Pro Gly Ile Arg Ile Val Asn Glu Lys Ala Arg Glu Arg Arg Ser
 115 120 125

Ser Arg Gly His Ser Ser Ser Asn Leu
 130 135

<210> 88

<211> 902

<212> PRT

<213> Homo sapiens

<400> 88

Met Leu Asp Ser Ser Asp Ser Ser Ser Gln Pro His Trp Ser Asn Glu
 1 5 10 15

Leu Ile Ala Glu Gln Leu Gln Gln Gln Val Ser Gln Leu Gln Asp Gln
 20 25 30

Leu Asp Ala Glu Leu Glu Asp Lys Arg Lys Val Leu Leu Glu Leu Ser
 35 40 45

Arg Glu Lys Ala Gln Asn Glu Asp Leu Lys Leu Glu Val Thr Asn Ile
 50 55 60

Leu Gln Lys His Lys Gln Glu Val Glu Leu Leu Gln Asn Ala Ala Thr
 65 70 75 80

Ile Ser Gln Pro Pro Asp Arg Gln Ser Glu Pro Ala Thr His Pro Ala
 85 90 95

Val Leu Gln Glu Asn Thr Gln Ile Glu Pro Ser Glu Pro Lys Asn Gln
 100 105 110

Glu Glu Lys Lys Leu Ser Gln Val Leu Asn Glu Leu Gln Val Ser His
 115 120 125

Ala Glu Thr Thr Leu Glu Leu Glu Lys Thr Arg Asp Met Leu Ile Leu
 130 135 140

Protein Complexes associated with APP-processing

Gln Arg Lys Ile Asn Val Cys Tyr Gln Glu Glu Leu Glu Ala Met Met
 145 150 155 160

Thr Lys Ala Asp Asn Asp Asn Arg Asp His Lys Glu Lys Leu Glu Arg
 165 170 175

Leu Thr Arg Leu Leu Asp Leu Lys Asn Asn Arg Ile Lys Gln Leu Glu
 180 185 190

Gly Ile Leu Arg Ser His Asp Leu Pro Thr Ser Glu Gln Leu Lys Asp
 195 200 205

Val Ala Tyr Gly Thr Arg Pro Leu Ser Leu Cys Leu Glu Thr Leu Pro
 210 215 220

Ala His Gly Asp Glu Asp Lys Val Asp Ile Ser Leu Leu His Gln Gly
 225 230 235 240

Glu Asn Leu Phe Glu Leu His Ile His Gln Ala Phe Leu Thr Ser Ala
 245 250 255

Ala Leu Ala Gln Ala Gly Asp Thr Gln Pro Thr Thr Phe Cys Thr Tyr
 260 265 270

Ser Phe Tyr Asp Phe Glu Thr His Cys Thr Pro Leu Ser Val Gly Pro
 275 280 285

Gln Pro Leu Tyr Asp Phe Thr Ser Gln Tyr Val Met Glu Thr Asp Ser
 290 295 300

Leu Phe Leu His Tyr Leu Gln Glu Ala Ser Ala Arg Leu Asp Ile His
 305 310 315 320

Gln Ala Met Ala Ser Glu His Ser Thr Leu Ala Ala Gly Trp Ile Cys
 325 330 335

Phe Asp Arg Val Leu Glu Thr Val Glu Lys Val His Gly Leu Ala Thr
 340 345 350

Leu Ile Gly Ala Gly Gly Glu Glu Phe Gly Val Leu Glu Tyr Trp Met
 355 360 365

Arg Leu Arg Phe Pro Ile Lys Pro Ser Leu Gln Ala Cys Asn Lys Arg
 370 375 380

Lys Lys Ala Gln Val Tyr Leu Ser Thr Asp Val Leu Gly Gly Arg Lys
 385 390 395 400

Ala Gln Glu Glu Glu Phe Arg Ser Glu Ser Trp Glu Pro Gln Asn Glu
 405 410 415

Protein Complexes associated with APP-processing
 Leu Trp Ile Glu Ile Thr Lys Cys Cys Gly Leu Arg Ser Arg Trp Leu
 420 425 430

Gly Thr Gln Pro Ser Pro Tyr Ala Val Tyr Arg Phe Phe Thr Phe Ser
 435 440 445

Asp His Asp Thr Ala Ile Ile Pro Ala Ser Asn Asn Pro Tyr Phe Arg
 450 455 460

Asp Gln Ala Arg Phe Pro Val Leu Val Thr Ser Asp Leu Asp His Tyr
 465 470 475 480

Leu Arg Arg Glu Ala Leu Ser Ile His Val Phe Asp Asp Glu Asp Leu
 485 490 495

Glu Pro Gly Ser Tyr Leu Gly Arg Ala Arg Val Pro Leu Leu Pro Leu
 500 505 510

Ala Lys Asn Glu Ser Ile Lys Gly Asp Phe Asn Leu Thr Asp Pro Ala
 515 520 525

Glu Lys Pro Asn Gly Ser Ile Gln Val Gln Leu Asp Trp Lys Phe Pro
 530 535 540

Tyr Ile Pro Pro Glu Ser Phe Leu Lys Pro Glu Ala Gln Thr Lys Gly
 545 550 555 560

Lys Asp Thr Lys Asp Ser Ser Lys Ile Ser Ser Glu Glu Glu Lys Ala
 565 570 575

Ser Phe Pro Ser Gln Asp Gln Met Ala Ser Pro Glu Val Pro Ile Glu
 580 585 590

Ala Gly Gln Tyr Arg Ser Lys Arg Lys Pro Pro His Gly Gly Glu Arg
 595 600 605

Lys Glu Lys Glu His Gln Val Val Ser Tyr Ser Arg Arg Lys His Gly
 610 615 620

Lys Arg Ile Gly Val Gln Gly Lys Asn Arg Met Glu Tyr Leu Ser Leu
 625 630 635 640

Asn Ile Leu Asn Gly Asn Thr Pro Gln Gln Val Asn Tyr Thr Glu Trp
 645 650 655

Lys Phe Ser Glu Thr Asn Ser Phe Ile Gly Asp Gly Phe Lys Asn Gln
 660 665 670

His Glu Glu Glu Glu Met Thr Leu Ser His Ser Ala Leu Lys Gln Lys
 675 680 685

Protein Complexes associated with APP-processing

Glu Pro Leu His Pro Val Asn Asp Lys Glu Ser Ser Glu Gln Gly Ser
 690 695 700

Glu Val Ser Glu Ala Gln Thr Thr Asp Ser Asp Asp Val Ile Val Pro
 705 710 715 720

Pro Met Ser Gln Lys Tyr Pro Lys Ala Asp Ser Glu Lys Met Cys Ile
 725 730 735

Glu Ile Val Ser Leu Ala Phe Tyr Pro Glu Ala Glu Val Met Ser Asp
 740 745 750

Glu Asn Ile Lys Gln Val Tyr Val Glu Tyr Lys Phe Tyr Asp Leu Pro
 755 760 765

Leu Ser Glu Thr Glu Thr Pro Val Ser Leu Arg Lys Pro Arg Ala Gly
 770 775 780

Glu Glu Ile His Phe His Phe Ser Lys Val Ile Asp Leu Asp Pro Gln
 785 790 795 800

Glu Gln Gln Gly Arg Arg Arg Phe Leu Phe Asp Met Leu Asn Gly Gln
 805 810 815

Asp Pro Asp Gln Gly His Leu Lys Phe Thr Val Val Ser Asp Pro Leu
 820 825 830

Asp Glu Glu Lys Lys Glu Cys Glu Glu Val Gly Tyr Ala Tyr Leu Gln
 835 840 845

Leu Trp Gln Ile Leu Glu Ser Gly Arg Asp Ile Leu Glu Gln Glu Leu
 850 855 860

Asp Ile Val Ser Pro Glu Asp Leu Ala Thr Pro Ile Gly Arg Leu Lys
 865 870 875 880

Val Ser Leu Gln Ala Ala Ala Val Leu His Ala Ile Tyr Lys Glu Met
 885 890 895

Thr Glu Asp Leu Phe Ser
 900

<210> 89

<211> 3460

<212> PRT

<213> Homo sapiens

<400> 89

Protein Complexes associated with APP-processing

Met Glu Arg Ser Gly Trp Ala Arg Gln Thr Phe Leu Leu Ala Leu Leu
 1 5 10 15

Leu Gly Ala Thr Leu Arg Ala Arg Ala Ala Ala Gly Tyr Tyr Pro Arg
 20 25 30

Phe Ser Pro Phe Phe Phe Leu Cys Thr His His Gly Glu Leu Glu Gly
 35 40 45

Asp Gly Glu Gln Gly Glu Val Leu Ile Ser Leu His Ile Ala Gly Asn
 50 55 60

Pro Thr Tyr Tyr Val Pro Gly Gln Glu Tyr His Val Thr Ile Ser Thr
 65 70 75 80

Ser Thr Phe Phe Asp Gly Leu Leu Val Thr Gly Leu Tyr Thr Ser Thr
 85 90 95

Ser Val Gln Ala Ser Gln Ser Ile Gly Gly Ser Ser Ala Phe Gly Phe
 100 105 110

Gly Ile Met Ser Asp His Gln Phe Gly Asn Gln Phe Met Cys Ser Val
 115 120 125

Val Ala Ser His Val Ser His Leu Pro Thr Thr Asn Leu Ser Phe Ile
 130 135 140

Trp Ile Ala Pro Pro Ala Gly Thr Gly Cys Val Asn Phe Met Ala Thr
 145 150 155 160

Ala Thr His Arg Gly Gln Val Ile Phe Lys Asp Ala Leu Ala Gln Gln
 165 170 175

Leu Cys Glu Gln Gly Ala Pro Thr Asp Val Thr Val His Pro His Leu
 180 185 190

Ala Glu Ile His Ser Asp Ser Ile Ile Leu Arg Asp Asp Phe Asp Ser
 195 200 205

Tyr His Gln Leu Gln Leu Asn Pro Asn Ile Trp Val Glu Cys Asn Asn
 210 215 220

Cys Glu Thr Gly Glu Gln Cys Gly Ala Ile Met His Gly Asn Ala Val
 225 230 235 240

Thr Phe Cys Glu Pro Tyr Gly Pro Arg Glu Leu Ile Thr Thr Gly Leu
 245 250 255

Asn Thr Thr Thr Ala Ser Val Leu Gln Phe Ser Ile Gly Ser Gly Ser
 260 265 270

Protein Complexes associated with APP-processing

Cys Arg Phe Ser Tyr Ser Asp Pro Ser Ile Ile Val Leu Tyr Ala Lys
 275 280 285

Asn Asn Ser Ala Asp Trp Ile Gln Leu Glu Lys Ile Arg Ala Pro Ser
 290 295 300

Asn Val Ser Thr Ile Ile His Ile Leu Tyr Leu Pro Glu Asp Ala Lys
 305 310 315 320

Gly Glu Asn Val Gln Phe Gln Trp Lys Gln Glu Asn Leu Arg Val Gly
 325 330 335

Glu Val Tyr Glu Ala Cys Trp Ala Leu Asp Asn Ile Leu Ile Ile Asn
 340 345 350

Ser Ala His Arg Gln Val Val Leu Glu Asp Ser Leu Asp Pro Val Asp
 355 360 365

Thr Gly Asn Trp Leu Phe Phe Pro Gly Ala Thr Val Lys His Ser Cys
 370 375 380

Gln Ser Asp Gly Asn Ser Ile Tyr Phe His Gly Asn Glu Gly Ser Glu
 385 390 395 400

Phe Asn Phe Ala Thr Thr Arg Asp Val Asp Leu Ser Thr Glu Asp Ile
 405 410 415

Gln Glu Gln Trp Ser Glu Glu Phe Glu Ser Gln Pro Thr Gly Trp Asp
 420 425 430

Val Leu Gly Ala Val Ile Gly Thr Glu Cys Gly Thr Ile Glu Ser Gly
 435 440 445

Leu Ser Met Val Phe Leu Lys Asp Gly Glu Arg Lys Leu Cys Thr Pro
 450 455 460

Ser Met Asp Thr Thr Gly Tyr Gly Asn Leu Arg Phe Tyr Phe Val Met
 465 470 475 480

Gly Gly Ile Cys Asp Pro Gly Asn Ser His Glu Asn Asp Ile Ile Leu
 485 490 495

Tyr Ala Lys Ile Glu Gly Arg Lys Glu His Ile Thr Leu Asp Thr Leu
 500 505 510

Ser Tyr Ser Ser Tyr Lys Val Pro Ser Leu Val Ser Val Val Ile Asn
 515 520 525

Pro Glu Leu Gln Thr Pro Ala Thr Lys Phe Cys Leu Arg Gln Lys Asn
 530 535 540

Protein Complexes associated with APP-processing

His Gln Gly His Asn Arg Asn Val Trp Ala Val Asp Phe Phe His Val
 545 550 555 560

Leu Pro Val Leu Pro Ser Thr Met Ser His Met Ile Gln Phe Ser Ile
 565 570 575

Asn Leu Gly Cys Gly Thr His Gln Pro Gly Asn Ser Val Ser Leu Glu
 580 585 590

Phe Ser Thr Asn His Gly Arg Ser Trp Ser Leu Leu His Thr Glu Cys
 595 600 605

Leu Pro Glu Ile Cys Ala Gly Pro His Leu Pro His Ser Thr Val Tyr
 610 615 620

Ser Ser Glu Asn Tyr Ser Gly Trp Asn Arg Ile Thr Ile Pro Leu Pro
 625 630 635 640

Asn Ala Ala Leu Thr Arg Asn Thr Arg Ile Arg Trp Arg Gln Thr Gly
 645 650 655

Pro Ile Leu Gly Asn Met Trp Ala Ile Asp Asn Val Tyr Ile Gly Pro
 660 665 670

Ser Cys Leu Lys Phe Cys Ser Gly Arg Gly Gln Cys Thr Arg His Gly
 675 680 685

Cys Lys Cys Asp Pro Gly Phe Ser Gly Pro Ala Cys Glu Met Ala Ser
 690 695 700

Gln Thr Phe Pro Met Phe Ile Ser Glu Ser Phe Gly Ser Ser Arg Leu
 705 710 715 720

Ser Ser Tyr His Asn Phe Tyr Ser Ile Arg Gly Ala Glu Val Ser Phe
 725 730 735

Gly Cys Gly Val Leu Ala Ser Gly Lys Ala Leu Val Phe Asn Lys Glu
 740 745 750

Gly Arg Arg Gln Leu Ile Thr Ser Phe Leu Asp Ser Ser Gln Ser Arg
 755 760 765

Phe Leu Gln Phe Thr Leu Arg Leu Gly Ser Lys Ser Val Leu Ser Thr
 770 775 780

Cys Arg Ala Pro Asp Gln Pro Gly Glu Gly Val Leu Leu His Tyr Ser
 785 790 795 800

Tyr Asp Asn Gly Ile Thr Trp Lys Leu Leu Glu His Tyr Ser Tyr Leu
 805 810 815

Protein Complexes associated with APP-processing

Ser Tyr His Glu Pro Arg Ile Ile Ser Val Glu Leu Pro Gly Asp Ala
 820 825 830

Lys Gln Phe Gly Ile Gln Phe Arg Trp Trp Gln Pro Tyr His Ser Ser
 835 840 845

Gln Arg Glu Asp Val Trp Ala Ile Asp Glu Ile Ile Met Thr Ser Val
 850 855 860

Leu Phe Asn Ser Ile Ser Leu Asp Phe Thr Asn Leu Val Glu Val Thr
 865 870 875 880

Gln Ser Leu Gly Phe Tyr Leu Gly Asn Val Gln Pro Tyr Cys Gly His
 885 890 895

Asp Trp Thr Leu Cys Phe Thr Gly Asp Ser Lys Leu Ala Ser Ser Met
 900 905 910

Arg Tyr Val Glu Thr Gln Ser Met Gln Ile Gly Ala Ser Tyr Met Ile
 915 920 925

Gln Phe Ser Leu Val Met Gly Cys Gly Gln Lys Tyr Thr Pro His Met
 930 935 940

Asp Asn Gln Val Lys Leu Glu Tyr Ser Thr Asn His Gly Leu Thr Trp
 945 950 955 960

His Leu Val Gln Glu Glu Cys Leu Pro Ser Met Pro Ser Cys Gln Glu
 965 970 975

Phe Thr Ser Ala Ser Ile Tyr His Ala Ser Glu Phe Thr Gln Trp Arg
 980 985 990

Arg Val Ile Val Leu Leu Pro Gln Lys Thr Trp Ser Ser Ala Thr Arg
 995 1000 1005

Phe Arg Trp Ser Gln Ser Tyr Tyr Thr Ala Gln Asp Glu Trp Ala
 1010 1015 1020

Leu Asp Ser Ile Tyr Ile Gly Gln Gln Cys Pro Asn Met Cys Ser
 1025 1030 1035

Gly His Gly Ser Cys Asp His Gly Ile Cys Arg Cys Asp Gln Gly
 1040 1045 1050

Tyr Gln Gly Thr Glu Cys His Pro Glu Ala Ala Leu Pro Ser Thr
 1055 1060 1065

Ile Met Ser Asp Phe Glu Asn Gln Asn Gly Trp Glu Ser Asp Trp
 1070 1075 1080

Protein Complexes associated with APP-processing

Gln	Glu	Val	Ile	Gly	Gly	Glu	Ile	Val	Lys	Pro	Glu	Gln	Gly	Cys
	1085					1090					1095			
Gly	Val	Ile	Ser	Ser	Gly	Ser	Ser	Leu	Tyr	Phe	Ser	Lys	Ala	Gly
	1100					1105					1110			
Lys	Arg	Gln	Leu	Val	Ser	Trp	Asp	Leu	Asp	Thr	Ser	Trp	Val	Asp
	1115					1120					1125			
Phe	Val	Gln	Phe	Tyr	Ile	Gln	Ile	Gly	Gly	Glu	Ser	Ala	Ser	Cys
	1130					1135					1140			
Asn	Lys	Pro	Asp	Ser	Arg	Glu	Glu	Gly	Val	Leu	Leu	Gln	Tyr	Ser
	1145					1150					1155			
Asn	Asn	Gly	Gly	Ile	Gln	Trp	His	Leu	Leu	Ala	Glu	Met	Tyr	Phe
	1160					1165					1170			
Ser	Asp	Phe	Ser	Lys	Pro	Arg	Phe	Val	Tyr	Leu	Glu	Leu	Pro	Ala
	1175					1180					1185			
Ala	Ala	Lys	Thr	Pro	Cys	Thr	Arg	Phe	Arg	Trp	Trp	Gln	Pro	Val
	1190					1195					1200			
Phe	Ser	Gly	Glu	Asp	Tyr	Asp	Gln	Trp	Ala	Val	Asp	Asp	Ile	Ile
	1205					1210					1215			
Ile	Leu	Ser	Glu	Lys	Gln	Lys	Gln	Ile	Ile	Pro	Val	Ile	Asn	Pro
	1220					1225					1230			
Thr	Leu	Pro	Gln	Asn	Phe	Tyr	Glu	Lys	Pro	Ala	Phe	Asp	Tyr	Pro
	1235					1240					1245			
Met	Asn	Gln	Met	Ser	Val	Trp	Leu	Met	Leu	Ala	Asn	Glu	Gly	Met
	1250					1255					1260			
Val	Lys	Asn	Glu	Thr	Phe	Cys	Ala	Ala	Thr	Pro	Ser	Ala	Met	Ile
	1265					1270					1275			
Phe	Gly	Lys	Ser	Asp	Gly	Asp	Arg	Phe	Ala	Val	Thr	Arg	Asp	Leu
	1280					1285					1290			
Thr	Leu	Lys	Pro	Gly	Tyr	Val	Leu	Gln	Phe	Lys	Leu	Asn	Ile	Gly
	1295					1300					1305			
Cys	Ala	Asn	Gln	Phe	Ser	Ser	Thr	Ala	Pro	Val	Leu	Leu	Gln	Tyr
	1310					1315					1320			
Ser	His	Asp	Ala	Gly	Met	Ser	Trp	Phe	Leu	Val	Lys	Glu	Gly	Cys
	1325					1330					1335			

Protein Complexes associated with APP-processing

Tyr Pro Ala Ser Ala Gly Lys Gly Cys Glu Gly Asn Ser Arg Glu
 1340 1345 1350
 Leu Ser Glu Pro Thr Met Tyr His Thr Gly Asp Phe Glu Glu Trp
 1355 1360 1365
 Thr Arg Ile Thr Ile Val Ile Pro Arg Ser Leu Ala Ser Ser Lys
 1370 1375 1380
 Thr Arg Phe Arg Trp Ile Gln Glu Ser Ser Ser Gln Lys Asn Val
 1385 1390 1395
 Pro Pro Phe Gly Leu Asp Gly Val Tyr Ile Ser Glu Pro Cys Pro
 1400 1405 1410
 Ser Tyr Cys Ser Gly His Gly Asp Cys Ile Ser Gly Val Cys Phe
 1415 1420 1425
 Cys Asp Leu Gly Tyr Thr Ala Ala Gln Gly Thr Cys Val Ser Asn
 1430 1435 1440
 Val Pro Asn His Asn Glu Met Phe Asp Arg Phe Glu Gly Lys Leu
 1445 1450 1455
 Ser Pro Leu Trp Tyr Lys Ile Thr Gly Ala Gln Val Gly Thr Gly
 1460 1465 1470
 Cys Gly Thr Leu Asn Asp Gly Lys Ser Leu Tyr Phe Asn Gly Pro
 1475 1480 1485
 Gly Lys Arg Glu Ala Arg Thr Val Pro Leu Asp Thr Arg Asn Ile
 1490 1495 1500
 Arg Leu Val Gln Phe Tyr Ile Gln Ile Gly Ser Lys Thr Ser Gly
 1505 1510 1515
 Ile Thr Cys Ile Lys Pro Arg Thr Arg Asn Glu Gly Leu Ile Val
 1520 1525 1530
 Gln Tyr Ser Asn Asp Asn Gly Ile Leu Trp His Leu Leu Arg Glu
 1535 1540 1545
 Leu Asp Phe Met Ser Phe Leu Glu Pro Gln Ile Ile Ser Ile Asp
 1550 1555 1560
 Leu Pro Gln Asp Ala Lys Thr Pro Ala Thr Ala Phe Arg Trp Trp
 1565 1570 1575
 Gln Pro Gln His Gly Lys His Ser Ala Gln Trp Ala Leu Asp Asp
 1580 1585 1590

Protein Complexes associated with APP-processing

Val	Leu	Ile	Gly	Met	Asn	Asp	Ser	Ser	Gln	Thr	Gly	Phe	Gln	Asp
	1595					1600					1605			
Lys	Phe	Asp	Gly	Ser	Ile	Asp	Leu	Gln	Ala	Asn	Trp	Tyr	Arg	Ile
	1610					1615					1620			
Gln	Gly	Gly	Gln	Val	Asp	Ile	Asp	Cys	Leu	Ser	Met	Asp	Thr	Ala
	1625					1630					1635			
Leu	Ile	Phe	Thr	Glu	Asn	Ile	Gly	Lys	Pro	Arg	Tyr	Ala	Glu	Thr
	1640					1645					1650			
Trp	Asp	Phe	His	Val	Ser	Ala	Ser	Thr	Phe	Leu	Gln	Phe	Glu	Met
	1655					1660					1665			
Ser	Met	Gly	Cys	Ser	Lys	Pro	Phe	Ser	Asn	Ser	His	Ser	Val	Gln
	1670					1675					1680			
Leu	Gln	Tyr	Ser	Leu	Asn	Asn	Gly	Lys	Asp	Trp	His	Leu	Val	Thr
	1685					1690					1695			
Glu	Glu	Cys	Val	Pro	Pro	Thr	Ile	Gly	Cys	Leu	His	Tyr	Thr	Glu
	1700					1705					1710			
Ser	Ser	Ile	Tyr	Thr	Ser	Glu	Arg	Phe	Gln	Asn	Trp	Lys	Arg	Ile
	1715					1720					1725			
Thr	Val	Tyr	Leu	Pro	Leu	Ser	Thr	Ile	Ser	Pro	Arg	Thr	Arg	Phe
	1730					1735					1740			
Arg	Trp	Ile	Gln	Ala	Asn	Tyr	Thr	Val	Gly	Ala	Asp	Ser	Trp	Ala
	1745					1750					1755			
Ile	Asp	Asn	Val	Val	Leu	Ala	Ser	Gly	Cys	Pro	Trp	Met	Cys	Ser
	1760					1765					1770			
Gly	Arg	Gly	Ile	Cys	Asp	Ala	Gly	Arg	Cys	Val	Cys	Asp	Arg	Gly
	1775					1780					1785			
Phe	Gly	Gly	Pro	Tyr	Cys	Val	Pro	Val	Val	Pro	Leu	Pro	Ser	Ile
	1790					1795					1800			
Leu	Lys	Asp	Asp	Phe	Asn	Gly	Asn	Leu	His	Pro	Asp	Leu	Trp	Pro
	1805					1810					1815			
Glu	Val	Tyr	Gly	Ala	Glu	Arg	Gly	Asn	Leu	Asn	Gly	Glu	Thr	Ile
	1820					1825					1830			
Lys	Ser	Gly	Thr	Ser	Leu	Ile	Phe	Lys	Gly	Glu	Gly	Leu	Arg	Met
	1835					1840					1845			

Protein Complexes associated with APP-processing

Leu Ile Ser Arg Asp Leu Asp Cys Thr Asn Thr Met Tyr Val Gln
1850 1855 1860

Phe Ser Leu Arg Phe Ile Ala Lys Ser Thr Pro Glu Arg Ser His
1865 1870 1875

Ser Ile Leu Leu Gln Phe Ser Ile Ser Gly Gly Ile Thr Trp His
1880 1885 1890

Leu Met Asp Glu Phe Tyr Phe Pro Gln Thr Thr Asn Ile Leu Phe
1895 1900 1905

Ile Asn Val Pro Leu Pro Tyr Thr Ala Gln Thr Asn Ala Thr Arg
1910 1915 1920

Phe Arg Leu Trp Gln Pro Tyr Asn Asn Gly Lys Lys Glu Glu Ile
1925 1930 1935

Trp Ile Val Asp Asp Phe Ile Ile Asp Gly Asn Asn Val Asn Asn
1940 1945 1950

Pro Val Met Leu Leu Asp Thr Phe Asp Phe Gly Pro Arg Glu Asp
1955 1960 1965

Asn Trp Phe Phe Tyr Pro Gly Gly Asn Ile Gly Leu Tyr Cys Pro
1970 1975 1980

Tyr Ser Ser Lys Gly Ala Pro Glu Glu Asp Ser Ala Met Val Phe
1985 1990 1995

Val Ser Asn Glu Val Gly Glu His Ser Ile Thr Thr Arg Asp Leu
2000 2005 2010

Asn Val Asn Glu Asn Thr Ile Ile Gln Phe Glu Ile Asn Val Gly
2015 2020 2025

Cys Ser Thr Asp Ser Ser Ser Ala Asp Pro Val Arg Leu Glu Phe
2030 2035 2040

Ser Arg Asp Phe Gly Ala Thr Trp His Leu Leu Leu Pro Leu Cys
2045 2050 2055

Tyr His Ser Ser Ser His Val Ser Ser Leu Cys Ser Thr Glu His
2060 2065 2070

His Pro Ser Ser Thr Tyr Tyr Ala Gly Thr Met Gln Gly Trp Arg
2075 2080 2085

Arg Glu Val Val His Phe Gly Lys Leu His Leu Cys Gly Ser Val
2090 2095 2100

Protein Complexes associated with APP-processing

Arg	Phe	Arg	Trp	Tyr	Gln	Gly	Phe	Tyr	Pro	Ala	Gly	Ser	Gln	Pro
	2105					2110					2115			
Val	Thr	Trp	Ala	Ile	Asp	Asn	Val	Tyr	Ile	Gly	Pro	Gln	Cys	Glu
	2120					2125					2130			
Glu	Met	Cys	Asn	Gly	Gln	Gly	Ser	Cys	Ile	Asn	Gly	Thr	Lys	Cys
	2135					2140					2145			
Ile	Cys	Asp	Pro	Gly	Tyr	Ser	Gly	Pro	Thr	Cys	Lys	Ile	Ser	Thr
	2150					2155					2160			
Lys	Asn	Pro	Asp	Phe	Leu	Lys	Asp	Asp	Phe	Glu	Gly	Gln	Leu	Glu
	2165					2170					2175			
Ser	Asp	Arg	Phe	Leu	Leu	Met	Ser	Gly	Gly	Lys	Pro	Ser	Arg	Lys
	2180					2185					2190			
Cys	Gly	Ile	Leu	Ser	Ser	Gly	Asn	Asn	Leu	Phe	Phe	Asn	Glu	Asp
	2195					2200					2205			
Gly	Leu	Arg	Met	Leu	Met	Thr	Arg	Asp	Leu	Asp	Leu	Ser	His	Ala
	2210					2215					2220			
Arg	Phe	Val	Gln	Phe	Phe	Met	Arg	Leu	Gly	Cys	Gly	Lys	Gly	Val
	2225					2230					2235			
Pro	Asp	Pro	Arg	Ser	Gln	Pro	Val	Leu	Leu	Gln	Tyr	Ser	Leu	Asn
	2240					2245					2250			
Gly	Gly	Leu	Ser	Trp	Ser	Leu	Leu	Gln	Glu	Phe	Leu	Phe	Ser	Asn
	2255					2260					2265			
Ser	Ser	Asn	Val	Gly	Arg	Tyr	Ile	Ala	Leu	Glu	Ile	Pro	Leu	Lys
	2270					2275					2280			
Ala	Arg	Ser	Gly	Ser	Thr	Arg	Leu	Arg	Trp	Trp	Gln	Pro	Ser	Glu
	2285					2290					2295			
Asn	Gly	His	Phe	Tyr	Ser	Pro	Trp	Val	Ile	Asp	Gln	Ile	Leu	Ile
	2300					2305					2310			
Gly	Gly	Asn	Ile	Ser	Gly	Asn	Thr	Val	Leu	Glu	Asp	Asp	Phe	Thr
	2315					2320					2325			
Thr	Leu	Asp	Ser	Arg	Lys	Trp	Leu	Leu	His	Pro	Gly	Gly	Thr	Lys
	2330					2335					2340			
Met	Pro	Val	Cys	Gly	Ser	Thr	Gly	Asp	Ala	Leu	Val	Phe	Ile	Glu
	2345					2350					2355			

Protein Complexes associated with APP-processing

Lys Ala Ser Thr Arg Tyr Val Val Ser Thr Asp Val Ala Val Asn
 2360 2365 2370

Glu Asp Ser Phe Leu Gln Ile Asp Phe Ala Ala Ser Cys Ser Val
 2375 2380 2385

Thr Asp Ser Cys Tyr Ala Ile Glu Leu Glu Tyr Ser Val Asp Leu
 2390 2395 2400

Gly Leu Ser Trp His Pro Leu Val Arg Asp Cys Leu Pro Thr Asn
 2405 2410 2415

Val Glu Cys Ser Arg Tyr His Leu Gln Arg Ile Leu Val Ser Asp
 2420 2425 2430

Thr Phe Asn Lys Trp Thr Arg Ile Thr Leu Pro Leu Pro Pro Tyr
 2435 2440 2445

Thr Arg Ser Gln Ala Thr Arg Phe Arg Trp His Gln Pro Ala Pro
 2450 2455 2460

Phe Asp Lys Gln Gln Thr Trp Ala Ile Asp Asn Val Tyr Ile Gly
 2465 2470 2475

Asp Gly Cys Ile Asp Met Cys Ser Gly His Gly Arg Cys Ile Gln
 2480 2485 2490

Gly Asn Cys Val Cys Asp Glu Gln Trp Gly Gly Leu Tyr Cys Asp
 2495 2500 2505

Asp Pro Glu Thr Ser Leu Pro Thr Gln Leu Lys Asp Asn Phe Asn
 2510 2515 2520

Arg Ala Pro Ser Ser Gln Asn Trp Leu Thr Val Asn Gly Gly Lys
 2525 2530 2535

Leu Ser Thr Val Cys Gly Ala Val Ala Ser Gly Met Ala Leu His
 2540 2545 2550

Phe Ser Gly Gly Cys Ser Arg Leu Leu Val Thr Val Asp Leu Asn
 2555 2560 2565

Leu Thr Asn Ala Glu Phe Ile Gln Phe Tyr Phe Met Tyr Gly Cys
 2570 2575 2580

Leu Ile Thr Pro Asn Asn Arg Asn Gln Gly Val Leu Leu Glu Tyr
 2585 2590 2595

Ser Val Asn Gly Gly Ile Thr Trp Asn Leu Leu Met Glu Ile Phe
 2600 2605 2610

Protein Complexes associated with APP-processing

Tyr Asp Gln Tyr Ser Lys Pro Gly Phe Val Asn Ile Leu Leu Pro
 2615 2620 2625

Pro Asp Ala Lys Glu Ile Ala Thr Arg Phe Arg Trp Trp Gln Pro
 2630 2635 2640

Arg His Asp Gly Leu Asp Gln Asn Asp Trp Ala Ile Asp Asn Val
 2645 2650 2655

Leu Ile Ser Gly Ser Ala Asp Gln Arg Thr Val Met Leu Asp Thr
 2660 2665 2670

Phe Ser Ser Ala Pro Val Pro Gln His Glu Arg Ser Pro Ala Asp
 2675 2680 2685

Ala Gly Pro Val Gly Arg Ile Ala Phe Asp Met Phe Met Glu Asp
 2690 2695 2700

Lys Thr Ser Val Asn Glu His Trp Leu Phe His Asp Asp Cys Thr
 2705 2710 2715

Val Glu Arg Phe Cys Asp Ser Pro Asp Gly Val Met Leu Cys Gly
 2720 2725 2730

Ser His Asp Gly Arg Glu Val Tyr Ala Val Thr His Asp Leu Thr
 2735 2740 2745

Pro Thr Glu Gly Trp Ile Met Gln Phe Lys Ile Ser Val Gly Cys
 2750 2755 2760

Lys Val Ser Glu Lys Ile Ala Gln Asn Gln Ile His Val Gln Tyr
 2765 2770 2775

Ser Thr Asp Phe Gly Val Ser Trp Asn Tyr Leu Val Pro Gln Cys
 2780 2785 2790

Leu Pro Ala Asp Pro Lys Cys Ser Gly Ser Val Ser Gln Pro Ser
 2795 2800 2805

Val Phe Phe Pro Thr Lys Gly Trp Lys Arg Ile Thr Tyr Pro Leu
 2810 2815 2820

Pro Glu Ser Leu Val Gly Asn Pro Val Arg Phe Arg Phe Tyr Gln
 2825 2830 2835

Lys Tyr Ser Asp Met Gln Trp Ala Ile Asp Asn Phe Tyr Leu Gly
 2840 2845 2850

Pro Gly Cys Leu Asp Asn Cys Arg Gly His Gly Asp Cys Leu Arg
 2855 2860 2865

Protein Complexes associated with APP-processing

Glu Gln Cys Ile Cys Asp Pro Gly Tyr Ser Gly Pro Asn Cys Tyr
 2870 2875 2880

Leu Thr His Thr Leu Lys Thr Phe Leu Lys Glu Arg Phe Asp Ser
 2885 2890 2895

Glu Glu Ile Lys Pro Asp Leu Trp Met Ser Leu Glu Gly Gly Ser
 2900 2905 2910

Thr Cys Thr Glu Cys Gly Ile Leu Ala Glu Asp Thr Ala Leu Tyr
 2915 2920 2925

Phe Gly Gly Ser Thr Val Arg Gln Ala Val Thr Gln Asp Leu Asp
 2930 2935 2940

Leu Arg Gly Ala Lys Phe Leu Gln Tyr Trp Gly Arg Ile Gly Ser
 2945 2950 2955

Glu Asn Asn Met Thr Ser Cys His Arg Pro Ile Cys Arg Lys Glu
 2960 2965 2970

Gly Val Leu Leu Asp Tyr Ser Thr Asp Gly Gly Ile Thr Trp Thr
 2975 2980 2985

Leu Leu His Glu Met Asp Tyr Gln Lys Tyr Ile Ser Val Arg His
 2990 2995 3000

Asp Tyr Ile Leu Leu Pro Glu Asp Ala Leu Thr Asn Thr Thr Arg
 3005 3010 3015

Leu Arg Trp Trp Gln Pro Phe Val Ile Ser Asn Gly Ile Val Val
 3020 3025 3030

Ser Gly Val Glu Arg Ala Gln Trp Ala Leu Asp Asn Ile Leu Ile
 3035 3040 3045

Gly Gly Ala Glu Ile Asn Pro Ser Gln Leu Val Asp Thr Phe Asp
 3050 3055 3060

Asp Glu Gly Thr Ser His Glu Glu Asn Trp Ser Phe Tyr Pro Asn
 3065 3070 3075

Ala Val Arg Thr Ala Gly Phe Cys Gly Asn Pro Ser Phe His Leu
 3080 3085 3090

Tyr Trp Pro Asn Lys Lys Lys Asp Lys Thr His Asn Ala Leu Ser
 3095 3100 3105

Ser Arg Glu Leu Ile Ile Gln Pro Gly Tyr Met Met Gln Phe Lys
 3110 3115 3120

Protein Complexes associated with APP-processing

Ile	Val	Val	Gly	Cys	Glu	Ala	Thr	Ser	Cys	Gly	Asp	Leu	His	Ser
	3125					3130					3135			
Val	Met	Leu	Glu	Tyr	Thr	Lys	Asp	Ala	Arg	Ser	Asp	Ser	Trp	Gln
	3140					3145					3150			
Leu	Val	Gln	Thr	Gln	Cys	Leu	Pro	Ser	Ser	Ser	Asn	Ser	Ile	Gly
	3155					3160					3165			
Cys	Ser	Pro	Phe	Gln	Phe	His	Glu	Ala	Thr	Ile	Tyr	Asn	Ser	Val
	3170					3175					3180			
Asn	Ser	Ser	Ser	Trp	Lys	Arg	Ile	Thr	Ile	Gln	Leu	Pro	Asp	His
	3185					3190					3195			
Val	Ser	Ser	Ser	Ala	Thr	Gln	Phe	Arg	Trp	Ile	Gln	Lys	Gly	Glu
	3200					3205					3210			
Glu	Thr	Glu	Lys	Gln	Ser	Trp	Ala	Ile	Asp	His	Val	Tyr	Ile	Gly
	3215					3220					3225			
Glu	Ala	Cys	Pro	Lys	Leu	Cys	Ser	Gly	His	Gly	Tyr	Cys	Thr	Thr
	3230					3235					3240			
Gly	Ala	Ile	Cys	Ile	Cys	Asp	Glu	Ser	Phe	Gln	Gly	Asp	Asp	Cys
	3245					3250					3255			
Ser	Val	Phe	Ser	His	Asp	Leu	Pro	Ser	Tyr	Ile	Lys	Asp	Asn	Phe
	3260					3265					3270			
Glu	Ser	Ala	Arg	Val	Thr	Glu	Ala	Asn	Trp	Glu	Thr	Ile	Gln	Gly
	3275					3280					3285			
Gly	Val	Ile	Gly	Ser	Gly	Cys	Gly	Gln	Leu	Ala	Pro	Tyr	Ala	His
	3290					3295					3300			
Gly	Asp	Ser	Leu	Tyr	Phe	Asn	Gly	Cys	Gln	Ile	Arg	Gln	Ala	Ala
	3305					3310					3315			
Thr	Lys	Pro	Leu	Asp	Leu	Thr	Arg	Ala	Ser	Lys	Ile	Met	Phe	Val
	3320					3325					3330			
Leu	Gln	Ile	Gly	Ser	Met	Ser	Gln	Thr	Asp	Ser	Cys	Asn	Ser	Asp
	3335					3340					3345			
Leu	Ser	Gly	Pro	His	Ala	Val	Asp	Lys	Ala	Val	Leu	Leu	Gln	Tyr
	3350					3355					3360			
Ser	Val	Asn	Asn	Gly	Ile	Thr	Trp	His	Val	Ile	Ala	Gln	His	Gln
	3365					3370					3375			

Protein Complexes associated with APP-processing
 Pro Lys Asp Phe Thr Gln Ala Gln Arg Val Ser Tyr Asn Val Pro
 3380 3385 3390

Leu Glu Ala Arg Met Lys Gly Val Leu Leu Arg Trp Trp Gln Pro
 3395 3400 3405

Arg His Asn Gly Thr Gly His Asp Gln Trp Ala Leu Asp His Val
 3410 3415 3420

Glu Val Val Leu Val Ser Thr Arg Lys Gln Asn Tyr Met Met Asn
 3425 3430 3435

Phe Ser Arg Gln His Gly Leu Arg His Phe Tyr Asn Arg Arg Arg
 3440 3445 3450

Arg Ser Leu Arg Arg Tyr Pro
 3455 3460

<210> 90

<211> 305

<212> PRT

<213> Homo sapiens

<400> 90

Met Ala Pro Leu Asp Leu Asp Lys Tyr Val Glu Ile Ala Arg Leu Cys
 1 5 10 15

Lys Tyr Leu Pro Glu Asn Asp Leu Lys Arg Leu Cys Asp Tyr Val Cys
 20 25 30

Asp Leu Leu Leu Glu Glu Ser Asn Val Gln Pro Val Ser Thr Pro Val
 35 40 45

Thr Val Cys Gly Asp Ile His Gly Gln Phe Tyr Asp Leu Cys Glu Leu
 50 55 60

Phe Arg Thr Gly Gly Gln Val Pro Asp Thr Asn Tyr Ile Phe Met Gly
 65 70 75 80

Asp Phe Val Asp Arg Gly Tyr Tyr Ser Leu Glu Thr Phe Thr Tyr Leu
 85 90 95

Leu Ala Leu Lys Ala Lys Trp Pro Asp Arg Ile Thr Leu Leu Arg Gly
 100 105 110

Asn His Glu Ser Arg Gln Ile Thr Gln Val Tyr Gly Phe Tyr Asp Glu
 115 120 125

Protein Complexes associated with APP-processing
 Cys Gln Thr Lys Tyr Gly Asn Ala Asn Ala Trp Arg Tyr Cys Thr Lys
 130 135 140

Val Phe Asp Met Leu Thr Val Ala Ala Leu Ile Asp Glu Gln Ile Leu
 145 150 155 160

Cys Val His Gly Gly Leu Ser Pro Asp Ile Lys Thr Leu Asp Gln Ile
 165 170 175

Arg Thr Ile Glu Arg Asn Gln Glu Ile Pro His Lys Gly Ala Phe Cys
 180 185 190

Asp Leu Val Trp Ser Asp Pro Glu Asp Val Asp Thr Trp Ala Ile Ser
 195 200 205

Pro Arg Gly Ala Gly Trp Leu Phe Gly Ala Lys Val Thr Asn Glu Phe
 210 215 220

Val His Ile Asn Asn Leu Lys Leu Ile Cys Arg Ala His Gln Leu Val
 225 230 235 240

His Glu Gly Tyr Lys Phe Met Phe Asp Glu Lys Leu Val Thr Val Trp
 245 250 255

Ser Ala Pro Asn Tyr Cys Tyr Arg Cys Gly Asn Ile Ala Ser Ile Met
 260 265 270

Val Phe Lys Asp Val Asn Thr Arg Glu Pro Lys Leu Phe Arg Ala Val
 275 280 285

Pro Asp Ser Glu Arg Val Ile Pro Pro Arg Thr Thr Thr Pro Tyr Phe
 290 295 300

Leu
 305

<210> 91

<211> 2214

<212> PRT

<213> Homo sapiens

<400> 91

Met Ala Thr Arg Ser Ser Arg Arg Glu Ser Arg Leu Pro Phe Leu Phe
 1 5 10 15

Thr Leu Val Ala Leu Leu Pro Pro Gly Ala Leu Cys Glu Val Trp Thr
 20 25 30

Protein Complexes associated with APP-processing

Gln Arg Leu His Gly Gly Ser Ala Pro Leu Pro Gln Asp Arg Gly Phe
 35 40 45

Leu Val Val Gln Gly Asp Pro Arg Glu Leu Arg Leu Trp Ala Arg Gly
 50 55 60

Asp Ala Arg Gly Ala Ser Arg Ala Asp Glu Lys Pro Leu Arg Arg Lys
 65 70 75 80

Arg Ser Ala Ala Leu Gln Pro Glu Pro Ile Lys Val Tyr Gly Gln Val
 85 90 95

Ser Leu Asn Asp Ser His Asn Gln Met Val Val His Trp Ala Gly Glu
 100 105 110

Lys Ser Asn Val Ile Val Ala Leu Ala Arg Asp Ser Leu Ala Leu Ala
 115 120 125

Arg Pro Lys Ser Ser Asp Val Tyr Val Ser Tyr Asp Tyr Gly Lys Ser
 130 135 140

Phe Lys Lys Ile Ser Asp Lys Leu Asn Phe Gly Leu Gly Asn Arg Ser
 145 150 155 160

Glu Ala Val Ile Ala Gln Phe Tyr His Ser Pro Ala Asp Asn Lys Arg
 165 170 175

Tyr Ile Phe Ala Asp Ala Tyr Ala Gln Tyr Leu Trp Ile Thr Phe Asp
 180 185 190

Phe Cys Asn Thr Leu Gln Gly Phe Ser Ile Pro Phe Arg Ala Ala Asp
 195 200 205

Leu Leu Leu His Ser Lys Ala Ser Asn Leu Leu Leu Gly Phe Asp Arg
 210 215 220

Ser His Pro Asn Lys Gln Leu Trp Lys Ser Asp Asp Phe Gly Gln Thr
 225 230 235 240

Trp Ile Met Ile Gln Glu His Val Lys Ser Phe Ser Trp Gly Ile Asp
 245 250 255

Pro Tyr Asp Lys Pro Asn Thr Ile Tyr Ile Glu Arg His Glu Pro Ser
 260 265 270

Gly Tyr Ser Thr Val Phe Arg Ser Thr Asp Phe Phe Gln Ser Arg Glu
 275 280 285

Asn Gln Glu Val Ile Leu Glu Glu Val Arg Asp Phe Gln Leu Arg Asp
 290 295 300

Protein Complexes associated with APP-processing

Lys Tyr Met Phe Ala Thr Lys Val Val His Leu Leu Gly Ser Glu Gln
 305 310 315 320

Gln Ser Ser Val Gln Leu Trp Val Ser Phe Gly Arg Lys Pro Met Arg
 325 330 335

Ala Ala Gln Phe Val Thr Arg His Pro Ile Asn Glu Tyr Tyr Ile Ala
 340 345 350

Asp Ala Ser Glu Asp Gln Val Phe Val Cys Val Ser His Ser Asn Asn
 355 360 365

Arg Thr Asn Leu Tyr Ile Ser Glu Ala Glu Gly Leu Lys Phe Ser Leu
 370 375 380

Ser Leu Glu Asn Val Leu Tyr Tyr Ser Pro Gly Gly Ala Gly Ser Asp
 385 390 395 400

Thr Leu Val Arg Tyr Phe Ala Asn Glu Pro Phe Ala Asp Phe His Arg
 405 410 415

Val Glu Gly Leu Gln Gly Val Tyr Ile Ala Thr Leu Ile Asn Gly Ser
 420 425 430

Met Asn Glu Glu Asn Met Arg Ser Val Ile Thr Phe Asp Lys Gly Gly
 435 440 445

Thr Trp Glu Phe Leu Gln Ala Pro Ala Phe Thr Gly Tyr Gly Glu Lys
 450 455 460

Ile Asn Cys Glu Leu Ser Gln Gly Cys Ser Leu His Leu Ala Gln Arg
 465 470 475 480

Leu Ser Gln Leu Leu Asn Leu Gln Leu Arg Arg Met Pro Ile Leu Ser
 485 490 495

Lys Glu Ser Ala Pro Gly Leu Ile Ile Ala Thr Gly Ser Val Gly Lys
 500 505 510

Asn Leu Ala Ser Lys Thr Asn Val Tyr Ile Ser Ser Ser Ala Gly Ala
 515 520 525

Arg Trp Arg Glu Ala Leu Pro Gly Pro His Tyr Tyr Thr Trp Gly Asp
 530 535 540

His Gly Gly Ile Ile Thr Ala Ile Ala Gln Gly Met Glu Thr Asn Glu
 545 550 555 560

Leu Lys Tyr Ser Thr Asn Glu Gly Glu Thr Trp Lys Thr Phe Ile Phe
 565 570 575

Protein Complexes associated with APP-processing

Ser Glu Lys Pro Val Phe Val Tyr Gly Leu Leu Thr Glu Pro Gly Glu
580 585 590

Lys Ser Thr Val Phe Thr Ile Phe Gly Ser Asn Lys Glu Asn Val His
595 600 605

Ser Trp Leu Ile Leu Gln Val Asn Ala Thr Asp Ala Leu Gly Val Pro
610 615 620

Cys Thr Glu Asn Asp Tyr Lys Leu Trp Ser Pro Ser Asp Glu Arg Gly
625 630 635 640

Asn Glu Cys Leu Leu Gly His Lys Thr Val Phe Lys Arg Arg Thr Pro
645 650 655

His Ala Thr Cys Phe Asn Gly Glu Asp Phe Asp Arg Pro Val Val Val
660 665 670

Ser Asn Cys Ser Cys Thr Arg Glu Asp Tyr Glu Cys Asp Phe Gly Phe
675 680 685

Lys Met Ser Glu Asp Leu Ser Leu Glu Val Cys Val Pro Asp Pro Glu
690 695 700

Phe Ser Gly Lys Ser Tyr Ser Pro Pro Val Pro Cys Pro Val Gly Ser
705 710 715 720

Thr Tyr Arg Arg Thr Arg Gly Tyr Arg Lys Ile Ser Gly Asp Thr Cys
725 730 735

Ser Gly Gly Asp Val Glu Ala Arg Leu Glu Gly Glu Leu Val Pro Cys
740 745 750

Pro Leu Ala Glu Glu Asn Glu Phe Ile Leu Tyr Ala Val Arg Lys Ser
755 760 765

Ile Tyr Arg Tyr Asp Leu Ala Ser Gly Ala Thr Glu Gln Leu Pro Leu
770 775 780

Thr Gly Leu Arg Ala Ala Val Ala Leu Asp Phe Asp Tyr Glu His Asn
785 790 795 800

Cys Leu Tyr Trp Ser Asp Leu Ala Leu Asp Val Ile Gln Arg Leu Cys
805 810 815

Leu Asn Gly Ser Thr Gly Gln Glu Val Ile Ile Asn Ser Gly Leu Glu
820 825 830

Thr Val Glu Ala Leu Ala Phe Glu Pro Leu Ser Gln Leu Leu Tyr Trp
835 840 845

Protein Complexes associated with APP-processing

Val Asp Ala Gly Phe Lys Lys Ile Glu Val Ala Asn Pro Asp Gly Asp
850 855 860

Phe Arg Leu Thr Ile Val Asn Ser Ser Val Leu Asp Arg Pro Arg Ala
865 870 875 880

Leu Val Leu Val Pro Gln Glu Gly Val Met Phe Trp Thr Asp Trp Gly
885 890 895

Asp Leu Lys Pro Gly Ile Tyr Arg Ser Asn Met Asp Gly Ser Ala Ala
900 905 910

Tyr His Leu Val Ser Glu Asp Val Lys Trp Pro Asn Gly Ile Ser Val
915 920 925

Asp Asp Gln Trp Ile Tyr Trp Thr Asp Ala Tyr Leu Glu Cys Ile Glu
930 935 940

Arg Ile Thr Phe Ser Gly Gln Gln Arg Ser Val Ile Leu Asp Asn Leu
945 950 955 960

Pro His Pro Tyr Ala Ile Ala Val Phe Lys Asn Glu Ile Tyr Trp Asp
965 970 975

Asp Trp Ser Gln Leu Ser Ile Phe Arg Ala Ser Lys Tyr Ser Gly Ser
980 985 990

Gln Met Glu Ile Leu Ala Asn Gln Leu Thr Gly Leu Met Asp Met Lys
995 1000 1005

Ile Phe Tyr Lys Gly Lys Asn Thr Gly Ser Asn Ala Cys Val Pro
1010 1015 1020

Arg Pro Cys Ser Leu Leu Cys Leu Pro Lys Ala Asn Asn Ser Arg
1025 1030 1035

Ser Cys Arg Cys Pro Glu Asp Val Ser Ser Ser Val Leu Pro Ser
1040 1045 1050

Gly Asp Leu Met Cys Asp Cys Pro Gln Gly Tyr Gln Leu Lys Asn
1055 1060 1065

Asn Thr Cys Val Lys Glu Glu Asn Thr Cys Leu Arg Asn Gln Tyr
1070 1075 1080

Arg Cys Ser Asn Gly Asn Cys Ile Asn Ser Ile Trp Trp Cys Asp
1085 1090 1095

Phe Asp Asn Asp Cys Gly Asp Met Ser Asp Glu Arg Asn Cys Pro
1100 1105 1110

Protein Complexes associated with APP-processing

Thr Thr Ile Cys Asp Leu Asp Thr Gln Phe Arg Cys Gln Glu Ser
 1115 1120 1125
 Gly Thr Cys Ile Pro Leu Ser Tyr Lys Cys Asp Leu Glu Asp Asp
 1130 1135 1140
 Cys Gly Asp Asn Ser Asp Glu Ser His Cys Glu Met His Gln Cys
 1145 1150 1155
 Arg Ser Asp Glu Tyr Asn Cys Ser Ser Gly Met Cys Ile Arg Ser
 1160 1165 1170
 Ser Trp Val Cys Asp Gly Asp Asn Asp Cys Arg Asp Trp Ser Asp
 1175 1180 1185
 Glu Ala Asn Cys Thr Ala Ile Tyr His Thr Cys Glu Ala Ser Asn
 1190 1195 1200
 Phe Gln Cys Arg Asn Gly His Cys Ile Pro Gln Arg Trp Ala Cys
 1205 1210 1215
 Asp Gly Asp Thr Asp Cys Gln Asp Gly Ser Asp Glu Asp Pro Val
 1220 1225 1230
 Asn Cys Glu Lys Lys Cys Asn Gly Phe Arg Cys Pro Asn Gly Thr
 1235 1240 1245
 Cys Ile Pro Ser Ser Lys His Cys Asp Gly Leu Arg Asp Cys Ser
 1250 1255 1260
 Asp Gly Ser Asp Glu Gln His Cys Glu Pro Leu Cys Thr His Phe
 1265 1270 1275
 Met Asp Phe Val Cys Lys Asn Arg Gln Gln Cys Leu Phe His Ser
 1280 1285 1290
 Met Val Cys Asp Gly Ile Ile Gln Cys Arg Asp Gly Ser Asp Glu
 1295 1300 1305
 Asp Ala Ala Phe Ala Gly Cys Ser Gln Asp Pro Glu Phe His Lys
 1310 1315 1320
 Val Cys Asp Glu Phe Gly Phe Gln Cys Gln Asn Gly Val Cys Ile
 1325 1330 1335
 Ser Leu Ile Trp Lys Cys Asp Gly Met Asp Asp Cys Gly Asp Tyr
 1340 1345 1350
 Ser Asp Glu Ala Asn Cys Glu Asn Pro Thr Glu Ala Pro Asn Cys
 1355 1360 1365

Protein Complexes associated with APP-processing

Ser Arg Tyr Phe Gln Phe Arg Cys Glu Asn Gly His Cys Ile Pro
1370 1375 1380

Asn Arg Trp Lys Cys Asp Arg Glu Asn Asp Cys Gly Asp Trp Ser
1385 1390 1395

Asp Glu Lys Asp Cys Gly Asp Ser His Ile Leu Pro Phe Ser Thr
1400 1405 1410

Pro Gly Pro Ser Thr Cys Leu Pro Asn Tyr Tyr Arg Cys Ser Ser
1415 1420 1425

Gly Thr Cys Val Met Asp Thr Trp Val Cys Asp Gly Tyr Arg Asp
1430 1435 1440

Cys Ala Asp Gly Ser Asp Glu Glu Ala Cys Pro Leu Leu Ala Asn
1445 1450 1455

Val Thr Ala Ala Ser Thr Pro Thr Gln Leu Gly Arg Cys Asp Arg
1460 1465 1470

Phe Glu Phe Glu Cys His Gln Pro Lys Thr Cys Ile Pro Asn Trp
1475 1480 1485

Lys Arg Cys Asp Gly His Gln Asp Cys Gln Asp Gly Arg Asp Glu
1490 1495 1500

Ala Asn Cys Pro Thr His Ser Thr Leu Thr Cys Met Ser Arg Glu
1505 1510 1515

Phe Gln Cys Glu Asp Gly Glu Ala Cys Ile Val Leu Ser Glu Arg
1520 1525 1530

Cys Asp Gly Phe Leu Asp Cys Ser Asp Glu Ser Asp Glu Lys Ala
1535 1540 1545

Cys Ser Asp Glu Leu Thr Val Tyr Lys Val Gln Asn Leu Gln Trp
1550 1555 1560

Thr Ala Asp Phe Ser Gly Asp Val Thr Leu Thr Trp Met Arg Pro
1565 1570 1575

Lys Lys Met Pro Ser Ala Ser Cys Val Tyr Asn Val Tyr Tyr Arg
1580 1585 1590

Val Val Gly Glu Ser Ile Trp Lys Thr Leu Glu Thr His Ser Asn
1595 1600 1605

Lys Thr Asn Thr Val Leu Lys Val Leu Lys Pro Asp Thr Thr Tyr
1610 1615 1620

Protein Complexes associated with APP-processing

Gln Val Lys Val Gln Val Gln Cys Leu Ser Lys Ala His Asn Thr
 1625 1630 1635

Asn Asp Phe Val Thr Leu Arg Thr Pro Glu Gly Leu Pro Asp Ala
 1640 1645 1650

Pro Arg Asn Leu Gln Leu Ser Leu Pro Arg Glu Ala Glu Gly Val
 1655 1660 1665

Ile Val Gly His Trp Ala Pro Pro Ile His Thr His Gly Leu Ile
 1670 1675 1680

Arg Glu Tyr Ile Val Glu Tyr Ser Arg Ser Gly Ser Lys Met Trp
 1685 1690 1695

Ala Ser Gln Arg Ala Ala Ser Asn Phe Thr Glu Ile Lys Asn Leu
 1700 1705 1710

Leu Val Asn Thr Leu Tyr Thr Val Arg Val Ala Ala Val Thr Ser
 1715 1720 1725

Arg Gly Ile Gly Asn Trp Ser Asp Ser Lys Ser Ile Thr Thr Ile
 1730 1735 1740

Lys Gly Lys Val Ile Pro Pro Pro Asp Ile His Ile Asp Ser Tyr
 1745 1750 1755

Gly Glu Asn Tyr Leu Ser Phe Thr Leu Thr Met Glu Ser Asp Ile
 1760 1765 1770

Lys Val Asn Gly Tyr Val Val Asn Leu Phe Trp Ala Phe Asp Thr
 1775 1780 1785

His Lys Gln Glu Arg Arg Thr Leu Asn Phe Arg Gly Ser Ile Leu
 1790 1795 1800

Ser His Lys Val Gly Asn Leu Thr Ala His Thr Ser Tyr Glu Ile
 1805 1810 1815

Ser Ala Trp Ala Lys Thr Asp Leu Gly Asp Ser Pro Leu Ala Phe
 1820 1825 1830

Glu His Val Met Thr Arg Gly Val Arg Pro Pro Ala Pro Ser Leu
 1835 1840 1845

Lys Ala Lys Ala Ile Asn Gln Thr Ala Val Glu Cys Thr Trp Thr
 1850 1855 1860

Gly Pro Arg Asn Val Val Tyr Gly Ile Phe Tyr Ala Thr Ser Phe
 1865 1870 1875

Protein Complexes associated with APP-processing

Leu Asp 1880 Leu Tyr Arg Asn Pro 1885 Lys Ser Leu Thr Thr 1890 Ser Leu His

Asn Lys 1895 Thr Val Ile Val Ser 1900 Lys Asp Glu Gln Tyr 1905 Leu Phe Leu

Val Arg 1910 Val Val Val Pro Tyr 1915 Gln Gly Pro Ser Ser 1920 Asp Tyr Val

Val Val 1925 Lys Met Ile Pro Asp 1930 Ser Arg Leu Pro Pro 1935 Arg His Leu

His Val 1940 Val His Thr Gly Lys 1945 Thr Ser Val Val Ile 1950 Lys Trp Glu

Ser Pro 1955 Tyr Asp Ser Pro Asp 1960 Gln Asp Leu Leu Tyr 1965 Ala Ile Ala

Val Lys 1970 Asp Leu Ile Arg Lys 1975 Thr Asp Arg Ser Tyr 1980 Lys Val Lys

Ser Arg 1985 Asn Ser Thr Val Glu 1990 Tyr Thr Leu Asn Lys 1995 Leu Glu Pro

Gly Gly 2000 Lys Tyr His Ile Ile 2005 Val Gln Leu Gly Asn 2010 Met Ser Lys

Asp Ser 2015 Ser Ile Lys Ile Thr 2020 Thr Val Ser Leu Ser 2025 Ala Pro Asp

Ala Leu 2030 Lys Ile Ile Thr Glu 2035 Asn Asp His Val Leu 2040 Leu Phe Trp

Lys Ser 2045 Leu Ala Leu Lys Glu 2050 Lys His Phe Asn Glu 2055 Ser Arg Gly

Tyr Glu 2060 Ile His Met Phe Asp 2065 Ser Ala Met Asn Ile 2070 Thr Ala Tyr

Leu Gly 2075 Asn Thr Thr Asp Asn 2080 Phe Phe Lys Ile Ser 2085 Asn Leu Lys

Met Gly 2090 His Asn Tyr Thr Phe 2095 Thr Val Gln Ala Arg 2100 Cys Leu Phe

Gly Asn 2105 Gln Ile Cys Gly Glu 2110 Pro Ala Ile Leu Leu 2115 Tyr Asp Glu

Leu Gly 2120 Ser Gly Ala Asp Ala 2125 Ser Ala Thr Gln Ala 2130 Ala Arg Ser

Protein Complexes associated with APP-processing
 Thr Asp Val Ala Ala Val Val Val Pro Ile Leu Phe Leu Ile Leu
 2135 2140 2145

Leu Ser Leu Gly Val Gly Phe Ala Ile Leu Tyr Thr Lys His Arg
 2150 2155 2160

Arg Leu Gln Ser Ser Phe Thr Ala Phe Ala Asn Ser His Tyr Ser
 2165 2170 2175

Ser Arg Leu Gly Ser Ala Ile Phe Ser Ser Gly Asp Asp Leu Gly
 2180 2185 2190

Glu Asp Asp Glu Asp Ala Pro Met Ile Thr Gly Phe Ser Asp Asp
 2195 2200 2205

Val Pro Met Val Ile Ala
 2210

<210> 92

<211> 229

<212> PRT

<213> Homo sapiens

<400> 92

Met Glu Gly Ala Ser Phe Gly Ala Gly Arg Ala Gly Ala Ala Leu Asp
 1 5 10 15

Pro Val Ser Phe Ala Arg Arg Pro Gln Thr Leu Leu Arg Val Ala Ser
 20 25 30

Trp Val Phe Ser Ile Ala Val Phe Gly Pro Ile Val Asn Glu Gly Tyr
 35 40 45

Val Asn Thr Asp Ser Gly Pro Glu Leu Arg Cys Val Phe Asn Gly Asn
 50 55 60

Ala Gly Ala Cys Arg Phe Gly Val Ala Leu Gly Leu Gly Ala Phe Leu
 65 70 75 80

Ala Cys Ala Ala Phe Leu Leu Leu Asp Val Arg Phe Gln Gln Ile Ser
 85 90 95

Ser Val Arg Asp Arg Arg Arg Ala Val Leu Leu Asp Leu Gly Phe Ser
 100 105 110

Gly Leu Trp Ser Phe Leu Trp Phe Val Gly Phe Cys Phe Leu Thr Asn
 115 120 125

Protein Complexes associated with APP-processing
 Gln Trp Gln Arg Thr Ala Pro Gly Pro Ala Thr Thr Gln Ala Gly Asp
 130 135 140

Ala Ala Arg Ala Ala Ile Ala Phe Ser Phe Phe Ser Ile Leu Ser Trp
 145 150 155 160

Val Ala Leu Thr Val Lys Ala Leu Gln Arg Phe Arg Leu Gly Thr Asp
 165 170 175

Met Ser Leu Phe Ala Thr Glu Gln Leu Ser Thr Gly Ala Ser Gln Ala
 180 185 190

Tyr Pro Gly Tyr Pro Val Gly Ser Gly Val Glu Gly Thr Glu Thr Tyr
 195 200 205

Gln Ser Pro Pro Phe Thr Glu Thr Leu Asp Thr Ser Pro Lys Gly Tyr
 210 215 220

Gln Val Pro Ala Tyr
 225

<210> 93

<211> 288

<212> PRT

<213> Homo sapiens

<400> 93

Met Lys Asp Arg Thr Gln Glu Leu Arg Thr Ala Lys Asp Ser Asp Asp
 1 5 10 15

Asp Asp Asp Val Ala Val Thr Val Asp Arg Asp Arg Phe Met Asp Glu
 20 25 30

Phe Phe Glu Gln Val Glu Glu Ile Arg Gly Phe Ile Asp Lys Ile Ala
 35 40 45

Glu Asn Val Glu Glu Val Lys Arg Lys His Ser Ala Ile Leu Ala Ser
 50 55 60

Pro Asn Pro Asp Glu Lys Thr Lys Glu Glu Leu Glu Glu Leu Met Ser
 65 70 75 80

Asp Ile Lys Lys Thr Ala Asn Lys Val Arg Ser Lys Leu Lys Ser Ile
 85 90 95

Glu Gln Ser Ile Glu Gln Glu Glu Gly Leu Asn Arg Ser Ser Ala Asp
 100 105 110

Protein Complexes associated with APP-processing

Leu Arg Ile Arg Lys Thr Gln His Ser Thr Leu Ser Arg Lys Phe Val
 115 120 125

Glu Val Met Ser Glu Tyr Asn Ala Thr Gln Ser Asp Tyr Arg Glu Arg
 130 135 140

Cys Lys Gly Arg Ile Gln Arg Gln Leu Glu Ile Thr Gly Arg Thr Thr
 145 150 155 160

Thr Ser Glu Glu Leu Glu Asp Met Leu Glu Ser Gly Asn Pro Ala Ile
 165 170 175

Phe Ala Ser Gly Ile Ile Met Asp Ser Ser Ile Ser Lys Gln Ala Leu
 180 185 190

Ser Glu Ile Glu Thr Arg His Ser Glu Ile Ile Lys Leu Glu Asn Ser
 195 200 205

Ile Arg Glu Leu His Asp Met Phe Met Asp Met Ala Met Leu Val Glu
 210 215 220

Ser Gln Gly Glu Met Ile Asp Arg Ile Glu Tyr Asn Val Glu His Ala
 225 230 235 240

Val Asp Tyr Val Glu Arg Ala Val Ser Asp Thr Lys Lys Ala Val Lys
 245 250 255

Tyr Gln Ser Lys Ala Arg Arg Lys Lys Ile Met Ile Ile Ile Cys Cys
 260 265 270

Val Ile Leu Gly Ile Val Ile Ala Ser Thr Val Gly Gly Ile Phe Ala
 275 280 285

<210> 94

<211> 717

<212> PRT

<213> Homo sapiens

<400> 94

Met Val Leu Ile Trp Arg Arg Ser Arg Tyr Leu Leu Arg Glu Ile Glu
 1 5 10 15

Ala Gln Trp Ser Ile Ser Ala Leu Trp Glu Gly Phe Gln Lys Trp Arg
 20 25 30

Asp Asn Leu Phe Leu Gln Ile Val Gln Leu Ile Gln His Val Tyr Ser
 35 40 45

Protein Complexes associated with APP-processing

Val Trp Thr Ala Ser Arg Thr Val Phe Ile Lys Ile Ile Val Thr Arg
50 55 60

His Thr Ser Thr Gly Gly Gly Phe Cys Asp Cys Gly Asp Thr Glu Ala
65 70 75 80

Trp Lys Thr Gly Pro Phe Cys Val Asn His Glu Pro Gly Arg Ala Gly
85 90 95

Thr Ile Lys Glu Asn Ser Arg Cys Pro Leu Asn Glu Glu Val Ile Val
100 105 110

Gln Ala Arg Lys Ile Phe Pro Ser Val Ile Lys Tyr Val Val Glu Met
115 120 125

Thr Ile Trp Glu Glu Glu Lys Glu Leu Pro Pro Glu Leu Gln Ile Arg
130 135 140

Glu Lys Asn Glu Arg Tyr Tyr Cys Val Leu Phe Asn Asp Glu His His
145 150 155 160

Ser Tyr Asp His Val Ile Tyr Ser Leu Gln Arg Ala Leu Asp Cys Glu
165 170 175

Leu Ala Glu Ala Gln Leu His Thr Thr Ala Ile Asp Lys Glu Gly Arg
180 185 190

Arg Ala Val Lys Ala Gly Ala Tyr Ala Ala Cys Gln Glu Ala Lys Glu
195 200 205

Asp Ile Lys Ser His Ser Glu Asn Val Ser Gln His Pro Leu His Val
210 215 220

Glu Val Leu His Ser Glu Ile Met Ala His Gln Lys Phe Ala Leu Arg
225 230 235 240

Leu Gly Ser Trp Met Asn Lys Ile Met Ser Tyr Ser Ser Asp Phe Arg
245 250 255

Gln Ile Phe Cys Gln Ala Cys Leu Arg Glu Glu Pro Asp Ser Glu Asn
260 265 270

Pro Cys Leu Ile Ser Arg Leu Met Leu Trp Asp Ala Lys Leu Tyr Lys
275 280 285

Gly Ala Arg Lys Ile Leu His Glu Leu Ile Phe Ser Ser Phe Phe Met
290 295 300

Glu Met Glu Tyr Lys Lys Leu Phe Ala Met Glu Phe Val Lys Tyr Tyr
305 310 315 320

Protein Complexes associated with APP-processing
Lys Gln Leu Gln Lys Glu Tyr Ile Ser Asp Asp His Asp Arg Ser Ile
325 330 335

Leu Val Leu Val Ala Gln Val Val Ala Glu Met Trp Arg Arg Asn Gly
580 585 590

Protein Complexes associated with APP-processing
 Leu Ser Leu Ile Ser Gln Val Phe Tyr Tyr Gln Asp Val Lys Cys Arg
 595 600 605

Glu Glu Met Tyr Asp Lys Asp Ile Ile Met Leu Gln Ile Gly Ala Ser
 610 615 620

Leu Met Asp Pro Asn Lys Phe Leu Leu Leu Val Leu Gln Arg Tyr Glu
 625 630 635 640

Leu Ala Glu Ala Phe Asn Lys Thr Ile Ser Thr Lys Asp Gln Asp Leu
 645 650 655

Ile Lys Gln Tyr Asn Thr Leu Ile Glu Glu Met Leu Gln Val Leu Ile
 660 665 670

Tyr Ile Val Gly Glu Arg Tyr Val Pro Gly Val Gly Asn Val Thr Lys
 675 680 685

Glu Glu Val Thr Met Arg Glu Ile Ile His Leu Leu Cys Ile Glu Pro
 690 695 700

Met Pro His Ser Ala Ile Ala Lys Asn Leu Pro Glu Asn
 705 710 715

<210> 95

<211> 616

<212> PRT

<213> Homo sapiens

<400> 95

Met Lys Ala Leu Arg Leu Ser Ala Ser Ala Leu Phe Cys Leu Leu Leu
 1 5 10 15

Ile Asn Gly Leu Gly Ala Ala Pro Pro Gly Arg Pro Glu Ala Gln Pro
 20 25 30

Pro Pro Leu Ser Ser Glu His Lys Glu Pro Val Ala Gly Asp Ala Val
 35 40 45

Pro Gly Pro Lys Asp Gly Ser Ala Pro Glu Val Arg Gly Ala Arg Asn
 50 55 60

Ser Glu Pro Gln Asp Glu Gly Glu Leu Phe Gln Gly Val Asp Pro Arg
 65 70 75 80

Ala Leu Ala Ala Val Leu Leu Gln Ala Leu Asp Arg Pro Ala Ser Pro
 85 90 95

Protein Complexes associated with APP-processing

Pro Ala Pro Ser Gly Ser Gln Gln Gly Pro Glu Glu Glu Ala Ala Glu
100 105 110

Ala Leu Leu Thr Glu Thr Val Arg Ser Gln Thr His Ser Leu Pro Ala
115 120 125

Ala Gly Glu Pro Glu Pro Ala Ala Pro Pro Arg Pro Gln Thr Pro Glu
130 135 140

Asn Gly Pro Glu Ala Ser Asp Pro Ser Glu Glu Leu Glu Ala Leu Ala
145 150 155 160

Ser Leu Leu Gln Glu Leu Arg Asp Phe Ser Pro Ser Ser Ala Lys Arg
165 170 175

Gln Gln Glu Thr Ala Ala Ala Glu Thr Glu Thr Arg Thr His Thr Leu
180 185 190

Thr Arg Val Asn Leu Glu Ser Pro Gly Pro Glu Arg Val Trp Arg Ala
195 200 205

Ser Trp Gly Glu Phe Gln Ala Arg Val Pro Glu Arg Ala Pro Leu Pro
210 215 220

Pro Pro Ala Pro Ser Gln Phe Gln Ala Arg Met Pro Asp Ser Gly Pro
225 230 235 240

Leu Pro Glu Thr His Lys Phe Gly Glu Gly Val Ser Ser Pro Lys Thr
245 250 255

His Leu Gly Glu Ala Leu Ala Pro Leu Ser Lys Ala Tyr Gln Gly Val
260 265 270

Ala Ala Pro Phe Pro Lys Ala Arg Arg Ala Glu Ser Ala Leu Leu Gly
275 280 285

Gly Ser Glu Ala Gly Glu Arg Leu Leu Gln Gln Gly Leu Ala Gln Val
290 295 300

Glu Ala Gly Arg Arg Gln Ala Glu Ala Thr Arg Gln Ala Ala Ala Gln
305 310 315 320

Glu Glu Arg Leu Ala Asp Leu Ala Ser Asp Leu Leu Leu Gln Tyr Leu
325 330 335

Leu Gln Gly Gly Ala Arg Gln Arg Gly Leu Gly Gly Arg Gly Leu Gln
340 345 350

Glu Ala Ala Glu Glu Arg Glu Ser Ala Arg Glu Glu Glu Glu Ala Glu
355 360 365

Protein Complexes associated with APP-processing
 Gln Glu Arg Arg Gly Gly Glu Glu Arg Val Gly Glu Glu Asp Glu Glu
 370 375 380

Ala Ala Glu Ala Ala Glu Ala Glu Ala Asp Glu Ala Glu Arg Ala Arg
 385 390 395 400

Gln Asn Ala Leu Leu Phe Ala Glu Glu Glu Asp Gly Glu Ala Gly Ala
 405 410 415

Glu Asp Lys Arg Ser Gln Glu Glu Thr Pro Gly His Arg Arg Lys Glu
 420 425 430

Ala Glu Gly Thr Glu Glu Gly Gly Glu Glu Glu Asp Asp Glu Glu Met
 435 440 445

Asp Pro Gln Thr Ile Asp Ser Leu Ile Glu Leu Ser Thr Lys Leu His
 450 455 460

Leu Pro Ala Asp Asp Val Val Ser Ile Ile Glu Glu Val Glu Glu Lys
 465 470 475 480

Arg Asn Arg Lys Lys Lys Ala Pro Pro Glu Pro Val Pro Pro Pro Arg
 485 490 495

Ala Ala Pro Ala Pro Thr His Val Arg Ser Pro Gln Pro Pro Pro Pro
 500 505 510

Pro Pro Ser Ala Arg Asp Glu Leu Pro Asp Trp Asn Glu Val Leu Pro
 515 520 525

Pro Trp Asp Arg Glu Glu Asp Glu Val Tyr Pro Pro Gly Pro Tyr His
 530 535 540

Pro Phe Pro Asn Tyr Ile Arg Pro Arg Thr Leu Gln Pro Pro Ser Ala
 545 550 555 560

Leu Arg Arg Arg His Tyr His His Ala Leu Pro Pro Ser Arg His Tyr
 565 570 575

Pro Gly Arg Glu Ala Gln Ala Arg His Ala Gln Gln Glu Glu Ala Glu
 580 585 590

Ala Glu Glu Arg Arg Leu Gln Glu Gln Glu Glu Leu Glu Asn Tyr Ile
 595 600 605

Glu His Val Leu Leu Arg Arg Pro
 610 615

<210> 96

<211> 749

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 96

Met Ala His Arg Lys Leu Glu Ser Val Gly Ser Gly Met Leu Asp His
 1 5 10 15

Arg Val Arg Pro Gly Pro Val Pro His Ser Gln Glu Pro Glu Ser Glu
 20 25 30

Asp Met Glu Leu Pro Leu Glu Gly Tyr Val Pro Glu Gly Leu Glu Leu
 35 40 45

Ala Ala Leu Arg Pro Glu Ser Pro Ala Pro Glu Glu Gln Glu Cys His
 50 55 60

Asn His Ser Pro Asp Gly Asp Ser Ser Ser Asp Tyr Val Asn Asn Thr
 65 70 75 80

Ser Glu Glu Glu Asp Tyr Asp Glu Gly Leu Pro Glu Glu Glu Glu Gly
 85 90 95

Ile Thr Tyr Tyr Ile Arg Tyr Cys Pro Glu Asp Asp Ser Tyr Leu Glu
 100 105 110

Gly Met Asp Cys Asn Gly Glu Glu Tyr Leu Ala His Ser Ala His Pro
 115 120 125

Val Asp Thr Asp Glu Cys Gln Glu Ala Val Glu Glu Trp Thr Asp Ser
 130 135 140

Ala Gly Pro His Pro His Gly His Glu Ala Glu Gly Ser Gln Asp Tyr
 145 150 155 160

Pro Asp Gly Gln Leu Pro Ile Pro Glu Asp Glu Pro Ser Val Leu Glu
 165 170 175

Ala His Asp Gln Glu Glu Asp Gly His Tyr Cys Ala Ser Lys Glu Gly
 180 185 190

Tyr Gln Asp Tyr Tyr Pro Glu Glu Ala Asn Gly Asn Thr Gly Ala Ser
 195 200 205

Pro Tyr Arg Leu Arg Arg Gly Asp Gly Asp Leu Glu Asp Gln Glu Glu
 210 215 220

Asp Ile Asp Gln Ile Val Ala Glu Ile Lys Met Ser Leu Ser Met Thr
 225 230 235 240

Protein Complexes associated with APP-processing

Ser Ile Thr Ser Ala Ser Glu Ala Ser Pro Glu His Gly Pro Glu Pro
245 250 255

Gly Pro Glu Asp Ser Val Glu Ala Cys Pro Pro Ile Lys Ala Ser Cys
260 265 270

Ser Pro Ser Arg His Glu Ala Arg Pro Lys Ser Leu Asn Leu Leu Pro
275 280 285

Glu Ala Lys His Pro Gly Asp Pro Gln Arg Gly Phe Lys Pro Lys Thr
290 295 300

Arg Thr Pro Glu Glu Arg Leu Lys Trp Pro His Glu Gln Val Cys Asn
305 310 315 320

Gly Leu Glu Gln Pro Arg Lys Gln Gln Arg Ser Asp Leu Asn Gly Pro
325 330 335

Val Asp Asn Asn Asn Ile Pro Glu Thr Lys Lys Val Ala Ser Phe Pro
340 345 350

Ser Phe Val Ala Val Pro Gly Pro Cys Glu Pro Glu Asp Leu Ile Asp
355 360 365

Gly Ile Ile Phe Ala Ala Asn Tyr Leu Gly Ser Thr Gln Leu Leu Ser
370 375 380

Glu Arg Asn Pro Ser Lys Asn Ile Arg Met Met Gln Ala Gln Glu Ala
385 390 395 400

Val Ser Arg Val Lys Arg Met Gln Lys Ala Ala Lys Ile Lys Lys Lys
405 410 415

Ala Asn Ser Glu Gly Asp Ala Gln Thr Leu Thr Glu Val Asp Leu Phe
420 425 430

Ile Ser Thr Gln Arg Ile Lys Val Leu Asn Ala Asp Thr Gln Glu Thr
435 440 445

Met Met Asp His Ala Leu Arg Thr Ile Ser Tyr Ile Ala Asp Ile Gly
450 455 460

Asn Ile Val Val Leu Met Ala Arg Arg Arg Met Pro Arg Ser Ala Ser
465 470 475 480

Gln Asp Cys Ile Glu Thr Thr Pro Gly Ala Gln Glu Gly Lys Lys Gln
485 490 495

Tyr Lys Met Ile Cys His Val Phe Glu Ser Glu Asp Ala Gln Leu Ile
500 505 510

Protein Complexes associated with APP-processing

Ala Gln Ser Ile Gly Gln Ala Phe Ser Val Ala Tyr Gln Glu Phe Leu
 515 520 525

Arg Ala Asn Gly Ile Asn Pro Glu Asp Leu Ser Gln Lys Glu Tyr Ser
 530 535 540

Asp Ile Ile Asn Thr Gln Glu Met Tyr Asn Asp Asp Leu Ile His Phe
 545 550 555 560

Ser Asn Ser Glu Asn Cys Lys Glu Leu Gln Leu Glu Lys His Lys Gly
 565 570 575

Glu Ile Leu Gly Val Val Val Val Glu Ser Gly Trp Gly Ser Ile Leu
 580 585 590

Pro Thr Val Ile Leu Ala Asn Met Met Asn Gly Gly Pro Ala Ala Arg
 595 600 605

Ser Gly Lys Leu Ser Ile Gly Asp Gln Ile Met Ser Ile Asn Gly Thr
 610 615 620

Ser Leu Val Gly Leu Pro Leu Ala Thr Cys Gln Gly Ile Ile Lys Gly
 625 630 635 640

Leu Lys Asn Gln Thr Gln Val Lys Leu Asn Ile Val Ser Cys Pro Pro
 645 650 655

Val Thr Thr Val Leu Ile Lys Arg Pro Asp Leu Lys Tyr Gln Leu Gly
 660 665 670

Phe Ser Val Gln Asn Gly Ile Ile Cys Ser Leu Met Arg Gly Gly Ile
 675 680 685

Ala Glu Arg Gly Gly Val Arg Val Gly His Arg Ile Ile Glu Ile Asn
 690 695 700

Gly Gln Ser Val Val Ala Thr Ala His Glu Lys Ile Val Gln Ala Leu
 705 710 715 720

Ser Asn Ser Val Gly Glu Ile His Met Lys Thr Met Pro Ala Ala Met
 725 730 735

Phe Arg Leu Leu Thr Gly Gln Glu Thr Pro Leu Tyr Ile
 740 745

<210> 97

<211> 1377

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 97

Met Asp Thr Ser Ser Val Gly Gly Leu Glu Leu Thr Asp Gln Thr Pro
 1 5 10 15
 Val Leu Leu Gly Ser Thr Ala Met Ala Thr Ser Leu Thr Asn Val Gly
 20 25 30
 Asn Ser Phe Ser Gly Pro Ala Asn Pro Leu Val Ser Arg Ser Asn Lys
 35 40 45
 Phe Gln Asn Ser Ser Val Glu Asp Asp Asp Asp Val Val Phe Ile Glu
 50 55 60
 Pro Val Gln Pro Pro Pro Ser Val Pro Val Val Ala Asp Gln Arg
 65 70 75 80
 Thr Ile Thr Phe Thr Ser Ser Lys Asn Glu Glu Leu Gln Gly Asn Asp
 85 90 95
 Ser Lys Ile Thr Pro Ser Ser Lys Glu Leu Ala Ser Gln Lys Gly Ser
 100 105 110
 Val Ser Glu Thr Ile Val Ile Asp Asp Glu Glu Asp Met Glu Thr Asn
 115 120 125
 Gln Gly Gln Glu Lys Asn Ser Ser Asn Phe Ile Glu Arg Arg Pro Pro
 130 135 140
 Glu Thr Lys Asn Arg Thr Asn Asp Val Asp Phe Ser Thr Ser Ser Phe
 145 150 155 160
 Ser Arg Ser Lys Val Asn Ala Gly Met Gly Asn Ser Gly Ile Thr Thr
 165 170 175
 Glu Pro Asp Ser Glu Ile Gln Ile Ala Asn Val Thr Thr Leu Glu Thr
 180 185 190
 Gly Val Ser Ser Val Asn Asp Gly Gln Leu Glu Asn Thr Asp Gly Arg
 195 200 205
 Asp Met Asn Leu Met Ile Thr His Val Thr Ser Leu Gln Asn Thr Asn
 210 215 220
 Leu Gly Asp Val Ser Asn Gly Leu Gln Ser Ser Asn Phe Gly Val Asn
 225 230 235 240
 Ile Gln Thr Tyr Thr Pro Ser Leu Thr Ser Gln Thr Lys Thr Gly Val
 245 250 255

Protein Complexes associated with APP-processing

Gly Pro Phe Asn Pro Gly Arg Met Asn Val Ala Gly Asp Val Phe Gln
 260 265 270

Asn Gly Glu Ser Ala Thr His His Asn Pro Asp Ser Trp Ile Ser Gln
 275 280 285

Ser Ala Ser Phe Pro Arg Asn Gln Lys Gln Pro Gly Val Asp Ser Leu
 290 295 300

Ser Pro Val Ala Ser Leu Pro Lys Gln Ile Phe Gln Pro Ser Val Gln
 305 310 315 320

Gln Gln Pro Thr Lys Pro Val Lys Val Thr Cys Ala Asn Cys Lys Lys
 325 330 335

Pro Leu Gln Lys Gly Gln Thr Ala Tyr Gln Arg Lys Gly Ser Ala His
 340 345 350

Leu Phe Cys Ser Thr Thr Cys Leu Ser Ser Phe Ser His Lys Pro Ala
 355 360 365

Pro Lys Lys Leu Cys Val Met Cys Lys Lys Asp Ile Thr Thr Met Lys
 370 375 380

Gly Thr Ile Val Ala Gln Val Asp Ser Ser Glu Ser Phe Gln Glu Phe
 385 390 395 400

Cys Ser Thr Ser Cys Leu Ser Leu Tyr Glu Asp Lys Gln Asn Pro Thr
 405 410 415

Lys Gly Ala Leu Asn Lys Ser Arg Cys Thr Ile Cys Gly Lys Leu Thr
 420 425 430

Glu Ile Arg His Glu Val Ser Phe Lys Asn Met Thr His Lys Leu Cys
 435 440 445

Ser Asp His Cys Phe Asn Arg Tyr Arg Met Ala Asn Gly Leu Ile Met
 450 455 460

Asn Cys Cys Glu Gln Cys Gly Glu Tyr Leu Pro Ser Lys Gly Ala Gly
 465 470 475 480

Asn Asn Val Leu Val Ile Asp Gly Gln Gln Lys Arg Phe Cys Cys Gln
 485 490 495

Ser Cys Val Ser Glu Tyr Lys Gln Val Gly Ser His Pro Ser Phe Leu
 500 505 510

Lys Glu Val Arg Asp His Met Gln Asp Ser Phe Leu Met Gln Pro Glu
 515 520 525

Protein Complexes associated with APP-processing

Lys Tyr Gly Lys Leu Thr Thr Cys Thr Gly Cys Arg Thr Gln Cys Arg
530 535 540

Phe Phe Asp Met Thr Gln Cys Ile Gly Pro Asn Gly Tyr Met Glu Pro
545 550 555 560

Tyr Cys Ser Thr Ala Cys Met Asn Ser His Lys Thr Lys Tyr Ala Lys
565 570 575

Ser Gln Ser Leu Gly Ile Ile Cys His Phe Cys Lys Arg Asn Ser Leu
580 585 590

Pro Gln Tyr Gln Ala Thr Met Pro Asp Gly Lys Leu Tyr Asn Phe Cys
595 600 605

Asn Ser Ser Cys Val Ala Lys Phe Gln Ala Leu Ser Met Gln Ser Ser
610 615 620

Pro Asn Gly Gln Phe Val Ala Pro Ser Asp Ile Gln Leu Lys Cys Asn
625 630 635 640

Tyr Cys Lys Asn Ser Phe Cys Ser Lys Pro Glu Ile Leu Glu Trp Glu
645 650 655

Asn Lys Val His Gln Phe Cys Ser Lys Thr Cys Ser Asp Asp Tyr Lys
660 665 670

Lys Leu His Cys Ile Val Thr Tyr Cys Glu Tyr Cys Gln Glu Glu Lys
675 680 685

Thr Leu His Glu Thr Val Asn Phe Ser Gly Val Lys Arg Pro Phe Cys
690 695 700

Ser Glu Gly Cys Lys Leu Leu Tyr Lys Gln Asp Phe Ala Arg Arg Leu
705 710 715 720

Gly Leu Arg Cys Val Thr Cys Asn Tyr Cys Ser Gln Leu Cys Lys Lys
725 730 735

Gly Ala Thr Lys Glu Leu Asp Gly Val Val Arg Asp Phe Cys Ser Glu
740 745 750

Asp Cys Cys Lys Lys Phe Gln Asp Trp Tyr Tyr Lys Ala Ala Arg Cys
755 760 765

Asp Cys Cys Lys Ser Gln Gly Thr Leu Lys Glu Arg Val Gln Trp Arg
770 775 780

Gly Glu Met Lys His Phe Cys Asp Gln His Cys Leu Leu Arg Phe Tyr
785 790 795 800

Protein Complexes associated with APP-processing
Cys Gln Gln Asn Glu Pro Asn Met Thr Thr Gln Lys Gly Pro Glu Asn
805 810 815

Ser Ala Pro Pro Pro Ser Pro Thr Pro Asn Lys Glu Met Lys Asn Lys
835 840 845

Pro His Met Gln Thr Lys Ser Cys Gln Thr Asp Asp Thr Trp Arg Thr
865 870 875 880

Glu Tyr Val Pro Val Pro Ile Pro Val Pro Val Tyr Ile Pro Val Pro
885 890 895

Met His Met Tyr Ser Gln Asn Ile Pro Val Pro Thr Thr Val Pro Val
900 905 910

Pro Val Pro Val Phe Leu Pro Ala Pro Leu Asp Ser Ser Glu
915 920 925

Lys Ile Pro Ala Ala Ile Glu Glu Leu Lys Ser Lys Val Ser Ser Asp
930 935 940

Ala 945 Leu Asp Thr Glu 950 Leu Thr Met Thr 955 Asp Met Met Ser Glu Asp 960

Glu Gly Lys Thr **Glu** Thr Thr Asn Ile **Asn** Ser Val Ile Ile **Glu** Thr
965 970 975

Asp Ile Ile Gly Ser Asp Leu Leu Lys Asn Ser Asp Pro Glu Thr Gln
980 985 990

Ser Ser Met Pro Asp Val Pro Tyr Glu Pro Asp Leu Asp Ile Glu Ile
995 1000 1005

Asp Phe Pro Arg Ala Ala Glu Glu Leu Asp Met Glu Asn Glu Phe
1010 1015 1020

Leu Leu Pro Pro Val Phe Gly Glu Glu Tyr Glu Glu Gln Pro Arg
1025 1030 1035

Pro Arg Ser Lys Lys Lys Gly Ala Lys Arg Lys Ala Val Ser Gly
1040 1045 1050

Tyr Gln Ser His Asp Asp Ser Ser Asp Asn Ser Glu Cys Ser Phe
1055 1060 1065

Protein Complexes associated with APP-processing

Pro Phe Lys Tyr Thr Tyr Gly Val Asn Ala Trp Lys His Trp Val
1070 1075 1080

Lys Thr Arg Gln Leu Asp Glu Asp Leu Leu Val Leu Asp Glu Leu
1085 1090 1095

Lys Ser Ser Lys Ser Val Lys Leu Lys Glu Asp Leu Leu Ser His
1100 1105 1110

Thr Thr Ala Glu Leu Asn Tyr Gly Leu Ala His Phe Val Asn Glu
1115 1120 1125

Ile Arg Arg Pro Asn Gly Glu Asn Tyr Ala Pro Asp Ser Ile Tyr
1130 1135 1140

Tyr Leu Cys Leu Gly Ile Gln Glu Tyr Leu Cys Gly Ser Asn Arg
1145 1150 1155

Lys Asp Asn Ile Phe Ile Asp Pro Gly Tyr Gln Thr Phe Glu Gln
1160 1165 1170

Glu Leu Asn Lys Ile Leu Arg Ser Trp Gln Pro Ser Ile Leu Pro
1175 1180 1185

Asp Gly Ser Ile Phe Ser Arg Val Glu Glu Asp Tyr Leu Trp Arg
1190 1195 1200

Ile Lys Gln Leu Gly Ser His Ser Pro Val Ala Leu Leu Asn Thr
1205 1210 1215

Leu Phe Tyr Phe Asn Thr Lys Tyr Phe Gly Leu Lys Thr Val Glu
1220 1225 1230

Gln His Leu Arg Leu Ser Phe Gly Thr Val Phe Arg His Trp Lys
1235 1240 1245

Lys Asn Pro Leu Thr Met Glu Asn Lys Ala Cys Leu Arg Tyr Gln
1250 1255 1260

Val Ser Ser Leu Cys Gly Thr Asp Asn Glu Asp Lys Ile Thr Thr
1265 1270 1275

Gly Lys Arg Lys His Glu Asp Asp Glu Pro Val Phe Glu Gln Ile
1280 1285 1290

Glu Asn Thr Ala Asn Pro Ser Arg Cys Pro Val Lys Met Phe Glu
1295 1300 1305

Cys Tyr Leu Ser Lys Ser Pro Gln Asn Leu Asn Gln Arg Met Asp
1310 1315 1320

Protein Complexes associated with APP-processing
 Val Phe Tyr Leu Gln Pro Glu Cys Ser Ser Ser Thr Asp Ser Pro
 1325 1330 1335

Val Trp Tyr Thr Ser Thr Ser Leu Asp Arg Asn Thr Leu Glu Asn
 1340 1345 1350

Met Leu Val Arg Val Leu Leu Val Lys Asp Ile Tyr Asp Lys Asp
 1355 1360 1365

Asn Tyr Glu Leu Asp Glu Asp Thr Asp
 1370 1375

<210> 98

<211> 179

<212> PRT

<213> Homo sapiens

<400> 98

Met Leu Ser Leu Asp Phe Leu Asp Asp Val Arg Arg Met Asn Lys Arg
 1 5 10 15

Gln Leu Tyr Tyr Gln Val Leu Asn Phe Gly Met Ile Val Ser Ser Ala
 20 25 30

Leu Met Ile Trp Lys Gly Leu Met Val Ile Thr Gly Ser Glu Ser Pro
 35 40 45

Ile Val Val Val Leu Ser Gly Ser Met Glu Pro Ala Phe His Arg Gly
 50 55 60

Asp Leu Leu Phe Leu Thr Asn Arg Val Glu Asp Pro Ile Arg Val Gly
 65 70 75 80

Glu Ile Val Val Phe Arg Ile Glu Gly Arg Glu Ile Pro Ile Val His
 85 90 95

Arg Val Leu Lys Ile His Glu Lys Gln Asn Gly His Ile Lys Phe Leu
 100 105 110

Thr Lys Gly Asp Asn Asn Ala Val Asp Asp Arg Gly Leu Tyr Lys Gln
 115 120 125

Gly Gln His Trp Leu Glu Lys Lys Asp Val Val Gly Arg Ala Arg Gly
 130 135 140

Phe Val Pro Tyr Ile Gly Ile Val Thr Ile Leu Met Asn Asp Tyr Pro
 145 150 155 160

Protein Complexes associated with APP-processing
 Lys Phe Lys Tyr Ala Val Leu Phe Leu Leu Gly Leu Phe Val Leu Val
 165 170 175

His Arg Glu

<210> 99

<211> 1798

<212> PRT

<213> Homo sapiens

<400> 99

Ala Glu Ser Asp Leu Gln Leu Ala Gln Ile Lys Cys Asn Leu Gly Arg
 1 5 10 15

Ala Val Gln Leu Gln Glu Leu Trp Pro Gly Gly Leu Phe Trp Thr Arg
 20 25 30

Lys Leu Ser Thr Tyr Ile Arg Leu Tyr Gly Arg Lys Phe Ser Lys Glu
 35 40 45

Asp His Val Leu Phe Ile Lys Leu Leu Tyr Glu Leu Val Ser Ile Pro
 50 55 60

Lys Leu Glu Ile Ser Met Met Gln Gly Phe Ala Arg Leu Leu Ile Asn
 65 70 75 80

Leu Leu Lys Lys Lys Glu Leu Leu Ser Arg Ala Asp Leu Glu Leu Pro
 85 90 95

Trp Arg Pro Leu Tyr Asp Met Val Glu Arg Ile Leu Tyr Ser Lys Thr
 100 105 110

Glu His Leu Gly Leu Asn Trp Phe Pro Asn Ser Val Glu Asn Ile Leu
 115 120 125

Lys Thr Leu Val Lys Ser Cys Arg Pro Tyr Phe Pro Ala Asp Ala Thr
 130 135 140

Ala Glu Met Leu Glu Glu Trp Arg Pro Leu Met Cys Pro Phe Asp Val
 145 150 155 160

Thr Met Gln Lys Ala Ile Thr Tyr Phe Glu Ile Phe Leu Pro Thr Ser
 165 170 175

Leu Pro Pro Glu Leu His His Lys Gly Phe Lys Leu Trp Phe Asp Glu
 180 185 190

Protein Complexes associated with APP-processing

Leu Ile Gly Leu Trp Val Ser Val Gln Asn Leu Pro Gln Trp Glu Gly
 195 200 205

Gln Leu Val Asn Leu Phe Ala Arg Leu Ala Thr Asp Asn Ile Gly Tyr
 210 215 220

Ile Asp Trp Asp Pro Tyr Val Pro Lys Ile Phe Thr Arg Ile Leu Arg
 225 230 235 240

Ser Leu Asn Leu Pro Val Gly Ser Ser Gln Val Leu Val Pro Arg Phe
 245 250 255

Leu Thr Asn Ala Tyr Asp Ile Gly His Ala Val Ile Trp Ile Thr Ala
 260 265 270

Met Met Gly Gly Pro Ser Lys Leu Val Gln Lys His Leu Ala Gly Leu
 275 280 285

Phe Asn Ser Ile Thr Ser Phe Tyr His Pro Ser Asn Asn Gly Arg Trp
 290 295 300

Leu Asn Lys Leu Met Lys Leu Leu Gln Arg Leu Pro Asn Ser Val Val
 305 310 315 320

Arg Arg Leu His Arg Glu Arg Tyr Lys Lys Pro Ser Trp Leu Thr Pro
 325 330 335

Val Pro Asp Ser His Lys Leu Thr Asp Gln Asp Val Thr Asp Phe Val
 340 345 350

Gln Cys Ile Ile Gln Pro Val Leu Leu Ala Met Phe Ser Lys Thr Gly
 355 360 365

Ser Leu Glu Ala Ala Gln Ala Leu Gln Asn Leu Ala Leu Met Arg Pro
 370 375 380

Glu Leu Val Ile Pro Pro Val Leu Glu Arg Thr Tyr Pro Ala Leu Glu
 385 390 395 400

Thr Leu Thr Glu Pro His Gln Leu Thr Ala Thr Leu Ser Cys Val Ile
 405 410 415

Gly Val Ala Arg Ser Leu Val Ser Gly Gly Arg Trp Phe Pro Glu Gly
 420 425 430

Pro Thr His Met Leu Pro Leu Leu Met Arg Ala Leu Pro Gly Val Asp
 435 440 445

Pro Asn Asp Phe Ser Lys Cys Met Ile Thr Phe Gln Phe Ile Ala Thr
 450 455 460

Protein Complexes associated with APP-processing

Phe Ser Thr Leu Val Pro Leu Val Asp Cys Ser Ser Val Leu Gln Glu
 465 470 475 480

Arg Asn Asp Leu Thr Glu Val Glu Arg Glu Leu Cys Ser Ala Thr Ala
 485 490 495

Glu Phe Glu Asp Phe Val Leu Gln Phe Met Asp Arg Cys Phe Gly Leu
 500 505 510

Ile Glu Ser Ser Thr Leu Glu Gln Thr Arg Glu Glu Thr Glu Thr Glu
 515 520 525

Lys Met Thr His Leu Glu Ser Leu Val Glu Leu Gly Leu Ser Ser Thr
 530 535 540

Phe Ser Thr Ile Leu Thr Gln Cys Ser Lys Glu Ile Phe Met Val Ala
 545 550 555 560

Leu Gln Lys Val Phe Asn Phe Ser Thr Ser His Ile Phe Glu Thr Arg
 565 570 575

Val Ala Gly Arg Met Val Ala Asp Met Cys Arg Ala Ala Val Lys Cys
 580 585 590

Cys Pro Glu Glu Ser Leu Lys Leu Phe Val Pro His Cys Cys Ser Val
 595 600 605

Ile Thr Gln Leu Thr Met Asn Asp Asp Val Leu Asn Asp Glu Glu Leu
 610 615 620

Asp Lys Glu Leu Leu Trp Asn Leu Gln Leu Leu Ser Glu Ile Thr Arg
 625 630 635 640

Val Asp Gly Arg Lys Leu Leu Leu Tyr Arg Glu Gln Leu Val Lys Ile
 645 650 655

Leu Gln Arg Thr Leu His Leu Thr Cys Lys Gln Gly Tyr Thr Leu Ser
 660 665 670

Cys Asn Leu Leu His His Leu Leu Arg Ser Thr Thr Leu Ile Tyr Pro
 675 680 685

Thr Glu Tyr Cys Ser Val Pro Gly Gly Phe Asp Lys Pro Pro Ser Glu
 690 695 700

Tyr Phe Pro Ile Lys Asp Trp Gly Lys Pro Gly Asp Leu Trp Asn Leu
 705 710 715 720

Gly Ile Gln Trp His Val Pro Ser Ser Glu Glu Val Ser Phe Ala Phe
 725 730 735

Protein Complexes associated with APP-processing
 Tyr Leu Leu Asp Ser Phe Leu Gln Pro Glu Leu Val Lys Leu Gln His
 740 745 750

Cys Gly Asp Gly Lys Leu Glu Met Ser Arg Asp Asp Ile Leu Gln Ser
 755 760 765

Leu Thr Ile Val His Asn Cys Leu Ile Gly Ser Gly Asn Leu Leu Pro
 770 775 780

Pro Leu Lys Gly Glu Pro Val Thr Asn Leu Val Pro Ser Met Val Ser
 785 790 795 800

Leu Glu Glu Thr Lys Leu Tyr Thr Gly Leu Glu Tyr Asp Leu Ser Arg
 805 810 815

Glu Asn His Arg Glu Val Ile Ala Thr Val Ile Arg Lys Leu Leu Asn
 820 825 830

His Ile Leu Asp Asn Ser Glu Asp Asp Thr Lys Ser Leu Phe Leu Ile
 835 840 845

Ile Lys Ile Ile Gly Asp Leu Leu Gln Phe Gln Gly Ser His Lys His
 850 855 860

Glu Phe Asp Ser Arg Trp Lys Ser Phe Asn Leu Val Lys Lys Ser Met
 865 870 875 880

Glu Asn Arg Leu His Gly Lys Lys Gln His Ile Arg Ala Leu Leu Ile
 885 890 895

Asp Arg Val Met Leu Gln His Glu Leu Arg Thr Leu Thr Val Glu Gly
 900 905 910

Cys Glu Tyr Lys Lys Ile His Gln Asp Met Ile Arg Asp Leu Leu Arg
 915 920 925

Leu Ser Thr Ser Ser Tyr Ser Gln Val Arg Asn Lys Ala Gln Gln Thr
 930 935 940

Phe Phe Ala Ala Leu Gly Ala Tyr Asn Phe Cys Cys Arg Asp Ile Ile
 945 950 955 960

Pro Leu Val Leu Glu Phe Leu Arg Pro Asp Arg Gln Gly Val Thr Gln
 965 970 975

Gln Gln Phe Lys Gly Ala Leu Tyr Cys Leu Leu Gly Asn His Ser Gly
 980 985 990

Val Cys Leu Ala Asn Leu His Asp Trp Asp Cys Ile Val Gln Thr Trp
 995 1000 1005

Protein Complexes associated with APP-processing

Pro Ala Ile val Ser Ser Gly Leu Ser Gln Ala Met Ser Leu Glu
1010 1015 1020

Lys Pro Ser Ile Val Arg Leu Phe Asp Asp Leu Ala Glu Lys Ile
1025 1030 1035

His Arg Gln Tyr Glu Thr Ile Gly Leu Asp Phe Thr Ile Pro Lys
1040 1045 1050

Ser Cys Val Glu Ile Ala Glu Leu Leu Gln Gln Ser Lys Asn Pro
1055 1060 1065

Ser Ile Asn Gln Ile Leu Leu Ser Pro Glu Lys Ile Lys Glu Gly
1070 1075 1080

Ile Lys Arg Gln Gln Glu Lys Asn Ala Asp Ala Leu Arg Asn Tyr
1085 1090 1095

Glu Asn Leu Val Asp Thr Leu Leu Asp Gly Val Glu Gln Arg Asn
1100 1105 1110

Leu Pro Trp Lys Phe Glu His Ile Gly Ile Gly Leu Leu Ser Leu
1115 1120 1125

Leu Leu Arg Asp Asp Arg Val Leu Pro Leu Arg Ala Ile Arg Phe
1130 1135 1140

Phe Val Glu Asn Leu Asn His Asp Ala Ile Val Val Arg Lys Met
1145 1150 1155

Ala Ile Ser Ala Val Ala Gly Ile Leu Lys Gln Leu Lys Arg Thr
1160 1165 1170

His Lys Lys Leu Thr Ile Asn Pro Cys Glu Ile Ser Gly Cys Pro
1175 1180 1185

Lys Pro Thr Gln Ile Ile Ala Gly Asp Arg Pro Asp Asn His Trp
1190 1195 1200

Leu His Tyr Asp Ser Lys Thr Ile Pro Arg Thr Lys Lys Glu Trp
1205 1210 1215

Glu Ser Ser Cys Phe Val Glu Lys Thr His Trp Gly Tyr Tyr Thr
1220 1225 1230

Trp Pro Lys Asn Met Val Val Tyr Ala Gly Val Glu Glu Gln Pro
1235 1240 1245

Lys Leu Gly Arg Ser Arg Glu Asp Met Thr Glu Ala Glu Gln Ile
1250 1255 1260

Protein Complexes associated with APP-processing

Ile Phe Asp His Phe Ser Asp Pro Lys Phe Val Glu Gln Leu Ile
 1265 1270 1275

Thr Phe Leu Ser Leu Glu Asp Arg Lys Gly Lys Asp Lys Phe Asn
 1280 1285 1290

Pro Arg Arg Phe Cys Leu Phe Lys Gly Ile Phe Arg Asn Phe Asp
 1295 1300 1305

Asp Ala Phe Leu Pro Val Leu Lys Pro His Leu Glu His Leu Val
 1310 1315 1320

Ala Asp Ser His Glu Ser Thr Gln Arg Cys Val Ala Glu Ile Ile
 1325 1330 1335

Ala Gly Leu Ile Arg Gly Ser Lys His Trp Thr Phe Glu Lys Val
 1340 1345 1350

Glu Lys Leu Trp Glu Leu Leu Cys Pro Leu Leu Arg Thr Ala Leu
 1355 1360 1365

Ser Asn Ile Thr Val Glu Thr Tyr Asn Asp Trp Gly Ala Cys Ile
 1370 1375 1380

Ala Thr Ser Cys Glu Ser Arg Asp Pro Arg Lys Leu His Trp Leu
 1385 1390 1395

Phe Glu Leu Leu Leu Glu Ser Pro Leu Ser Gly Glu Gly Gly Ser
 1400 1405 1410

Phe Val Asp Ala Cys Arg Leu Tyr Val Leu Gln Gly Gly Leu Ala
 1415 1420 1425

Gln Gln Glu Trp Arg Val Pro Glu Leu Leu His Arg Leu Leu Lys
 1430 1435 1440

Tyr Leu Glu Pro Lys Leu Thr Gln Val Tyr Lys Asn Val Arg Glu
 1445 1450 1455

Arg Ile Gly Ser Val Leu Thr Tyr Ile Phe Met Ile Asp Val Ser
 1460 1465 1470

Leu Pro Asn Thr Thr Pro Thr Ile Ser Pro His Val Pro Glu Phe
 1475 1480 1485

Thr Ala Arg Ile Leu Glu Lys Leu Lys Pro Leu Met Asp Val Asp
 1490 1495 1500

Glu Glu Ile Gln Asn His Val Met Glu Glu Asn Gly Ile Gly Glu
 1505 1510 1515

Protein Complexes associated with APP-processing

Glu	Asp	Glu	Arg	Thr	Gln	Gly	Ile	Lys	Leu	Leu	Lys	Thr	Ile	Leu
	1520					1525					1530			
Lys	Trp	Leu	Met	Ala	Ser	Ala	Gly	Arg	Ser	Phe	Ser	Thr	Ala	Val
	1535					1540					1545			
Thr	Glu	Gln	Leu	Gln	Leu	Leu	Pro	Leu	Phe	Phe	Lys	Ile	Ala	Pro
	1550					1555					1560			
Val	Glu	Asn	Asp	Asn	Ser	Tyr	Asp	Glu	Leu	Lys	Arg	Asp	Ala	Lys
	1565					1570					1575			
Leu	Cys	Leu	Ser	Leu	Met	Ser	Gln	Gly	Leu	Leu	Tyr	Pro	His	Gln
	1580					1585					1590			
Val	Pro	Leu	Val	Leu	Gln	Val	Leu	Lys	Gln	Thr	Ala	Arg	Ser	Ser
	1595					1600					1605			
Ser	Trp	His	Ala	Arg	Tyr	Thr	Val	Leu	Thr	Tyr	Leu	Gln	Thr	Met
	1610					1615					1620			
Val	Phe	Tyr	Asn	Leu	Phe	Ile	Phe	Leu	Asn	Asn	Glu	Asp	Ala	Val
	1625					1630					1635			
Lys	Asp	Ile	Arg	Trp	Leu	Val	Ile	Ser	Leu	Leu	Glu	Asp	Glu	Gln
	1640					1645					1650			
Leu	Glu	Val	Arg	Glu	Met	Ala	Ala	Thr	Thr	Leu	Ser	Gly	Leu	Leu
	1655					1660					1665			
Gln	Cys	Asn	Phe	Leu	Thr	Met	Asp	Ser	Pro	Met	Gln	Ile	His	Phe
	1670					1675					1680			
Glu	Gln	Leu	Cys	Lys	Thr	Lys	Leu	Pro	Lys	Lys	Arg	Lys	Arg	Asp
	1685					1690					1695			
Pro	Gly	Ser	Val	Gly	Asp	Thr	Ile	Pro	Ser	Ala	Glu	Leu	Val	Lys
	1700					1705					1710			
Arg	His	Ala	Gly	Val	Leu	Gly	Leu	Gly	Ala	Cys	Val	Leu	Ser	Ser
	1715					1720					1725			
Pro	Tyr	Asp	Val	Pro	Thr	Trp	Met	Pro	Gln	Leu	Leu	Met	Asn	Leu
	1730					1735					1740			
Ser	Ala	His	Leu	Asn	Asp	Pro	Gln	Pro	Ile	Glu	Met	Thr	Val	Lys
	1745					1750					1755			
Lys	Thr	Leu	Ser	Asn	Phe	Arg	Arg	Thr	His	His	Asp	Asn	Trp	Gln
	1760					1765					1770			

Protein Complexes associated with APP-processing
 Glu His Lys Gln Gln Phe Thr Asp Asp Gln Leu Leu Val Leu Thr
 1775 1780 1785

Asp Leu Leu Val Ser Pro Cys Tyr Tyr Ala
 1790 1795

<210> 100

<211> 180

<212> PRT

<213> Homo sapiens

<400> 100

Gly Asn Ile Phe Gly Asn Leu Leu Lys Ser Leu Ile Gly Lys Lys Glu
 1 5 10 15

Met Arg Ile Leu Met Val Gly Leu Asp Ala Ala Gly Lys Thr Thr Ile
 20 25 30

Leu Tyr Lys Leu Lys Leu Gly Glu Ile Val Thr Thr Ile Pro Thr Ile
 35 40 45

Gly Phe Asn Val Glu Thr Val Glu Tyr Lys Asn Ile Ser Phe Thr Val
 50 55 60

Trp Asp Val Gly Gly Gln Asp Lys Ile Arg Pro Leu Trp Arg His Tyr
 65 70 75 80

Phe Gln Asn Thr Gln Gly Leu Ile Phe Val Val Asp Ser Asn Asp Arg
 85 90 95

Glu Arg Val Asn Glu Ala Arg Glu Glu Leu Met Arg Met Leu Ala Glu
 100 105 110

Asp Glu Leu Arg Asp Ala Val Leu Leu Val Phe Ala Asn Lys Gln Asp
 115 120 125

Leu Pro Asn Ala Met Asn Ala Ala Glu Ile Thr Asp Lys Leu Gly Leu
 130 135 140

His Ser Leu Arg His Arg Asn Trp Tyr Ile Gln Ala Thr Cys Ala Thr
 145 150 155 160

Ser Gly Asp Gly Leu Tyr Glu Gly Leu Asp Trp Leu Ala Asn Gln Leu
 165 170 175

Lys Asn Lys Lys
 180

Protein Complexes associated with APP-processing

<210> 101

<211> 1280

<212> PRT

<213> Homo sapiens

<400> 101

Met Asp Leu Glu Gly Asp Arg Asn Gly Gly Ala Lys Lys Lys Asn Phe
 1 5 10 15

Phe Lys Leu Asn Asn Lys Ser Glu Lys Asp Lys Lys Glu Lys Lys Pro
 20 25 30

Thr Val Ser Val Phe Ser Met Phe Arg Tyr Ser Asn Trp Leu Asp Lys
 35 40 45

Leu Tyr Met Val Val Gly Thr Leu Ala Ala Ile Ile His Gly Ala Gly
 50 55 60

Leu Pro Leu Met Met Leu Val Phe Gly Glu Met Thr Asp Ile Phe Ala
 65 70 75 80

Asn Ala Gly Asn Leu Glu Asp Leu Met Ser Asn Ile Thr Asn Arg Ser
 85 90 95

Asp Ile Asn Asp Thr Gly Phe Phe Met Asn Leu Glu Glu Asp Met Thr
 100 105 110

Arg Tyr Ala Tyr Tyr Tyr Ser Gly Ile Gly Ala Gly Val Leu Val Ala
 115 120 125

Ala Tyr Ile Gln Val Ser Phe Trp Cys Leu Ala Ala Gly Arg Gln Ile
 130 135 140

His Lys Ile Arg Lys Gln Phe Phe His Ala Ile Met Arg Gln Glu Ile
 145 150 155 160

Gly Trp Phe Asp Val His Asp Val Gly Glu Leu Asn Thr Arg Leu Thr
 165 170 175

Asp Asp Val Ser Lys Ile Asn Glu Gly Ile Gly Asp Lys Ile Gly Met
 180 185 190

Phe Phe Gln Ser Met Ala Thr Phe Phe Thr Gly Phe Ile Val Gly Phe
 195 200 205

Thr Arg Gly Trp Lys Leu Thr Leu Val Ile Leu Ala Ile Ser Pro Val
 210 215 220

Protein Complexes associated with APP-processing

Leu Gly Leu Ser Ala Ala Val Trp Ala Lys Ile Leu Ser Ser Phe Thr
 225 230 235 240

Asp Lys Glu Leu Leu Ala Tyr Ala Lys Ala Gly Ala Val Ala Glu Glu
 245 250 255

Val Leu Ala Ala Ile Arg Thr Val Ile Ala Phe Gly Gly Gln Lys Lys
 260 265 270

Glu Leu Glu Arg Tyr Asn Lys Asn Leu Glu Glu Ala Lys Arg Ile Gly
 275 280 285

Ile Lys Lys Ala Ile Thr Ala Asn Ile Ser Ile Gly Ala Ala Phe Leu
 290 295 300

Leu Ile Tyr Ala Ser Tyr Ala Leu Ala Phe Trp Tyr Gly Thr Thr Leu
 305 310 315 320

Val Leu Ser Gly Glu Tyr Ser Ile Gly Gln Val Leu Thr Val Phe Phe
 325 330 335

Ser Val Leu Ile Gly Ala Phe Ser Val Gly Gln Ala Ser Pro Ser Ile
 340 345 350

Glu Ala Phe Ala Asn Ala Arg Gly Ala Ala Tyr Glu Ile Phe Lys Ile
 355 360 365

Ile Asp Asn Lys Pro Ser Ile Asp Ser Tyr Ser Lys Ser Gly His Lys
 370 375 380

Pro Asp Asn Ile Lys Gly Asn Leu Glu Phe Arg Asn Val His Phe Ser
 385 390 395 400

Tyr Pro Ser Arg Lys Glu Val Lys Ile Leu Lys Gly Leu Asn Leu Lys
 405 410 415

Val Gln Ser Gly Gln Thr Val Ala Leu Val Gly Asn Ser Gly Cys Gly
 420 425 430

Lys Ser Thr Thr Val Gln Leu Met Gln Arg Leu Tyr Asp Pro Thr Glu
 435 440 445

Gly Met Val Ser Val Asp Gly Gln Asp Ile Arg Thr Ile Asn Val Arg
 450 455 460

Phe Leu Arg Glu Ile Ile Gly Val Val Ser Gln Glu Pro Val Leu Phe
 465 470 475 480

Ala Thr Thr Ile Ala Glu Asn Ile Arg Tyr Gly Arg Glu Asn Val Thr
 485 490 495

Protein Complexes associated with APP-processing

Met Asp Glu Ile Glu Lys Ala Val Lys Glu Ala Asn Ala Tyr Asp Phe
 500 505 510

Ile Met Lys Leu Pro His Lys Phe Asp Thr Leu Val Gly Glu Arg Gly
 515 520 525

Ala Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile Ala Ile Ala Arg Ala
 530 535 540

Leu Val Arg Asn Pro Lys Ile Leu Leu Leu Asp Glu Ala Thr Ser Ala
 545 550 555 560

Leu Asp Thr Glu Ser Glu Ala Val Val Gln Val Ala Leu Asp Lys Ala
 565 570 575

Arg Lys Gly Arg Thr Thr Ile Val Ile Ala His Arg Leu Ser Thr Val
 580 585 590

Arg Asn Ala Asp Val Ile Ala Gly Phe Asp Asp Gly Val Ile Val Glu
 595 600 605

Lys Gly Asn His Asp Glu Leu Met Lys Glu Lys Gly Ile Tyr Phe Lys
 610 615 620

Leu Val Thr Met Gln Thr Ala Gly Asn Glu Val Glu Leu Glu Asn Ala
 625 630 635 640

Ala Asp Glu Ser Lys Ser Glu Ile Asp Ala Leu Glu Met Ser Ser Asn
 645 650 655

Asp Ser Arg Ser Ser Leu Ile Arg Lys Arg Ser Thr Arg Arg Ser Val
 660 665 670

Arg Gly Ser Gln Ala Gln Asp Arg Lys Leu Ser Thr Lys Glu Ala Leu
 675 680 685

Asp Glu Ser Ile Pro Pro Val Ser Phe Trp Arg Ile Met Lys Leu Asn
 690 695 700

Leu Thr Glu Trp Pro Tyr Phe Val Val Gly Val Phe Cys Ala Ile Ile
 705 710 715 720

Asn Gly Gly Leu Gln Pro Ala Phe Ala Ile Ile Phe Ser Lys Ile Ile
 725 730 735

Gly Val Phe Thr Arg Ile Asp Asp Pro Glu Thr Lys Arg Gln Asn Ser
 740 745 750

Asn Leu Phe Ser Leu Leu Phe Leu Ala Leu Gly Ile Ile Ser Phe Ile
 755 760 765

Protein Complexes associated with APP-processing

Thr Phe Phe Leu Gln Gly Phe Thr Phe Gly Lys Ala Gly Glu Ile Leu
 770 775 780

Thr Lys Arg Leu Arg Tyr Met Val Phe Arg Ser Met Leu Arg Gln Asp
 785 790 795 800

Val Ser Trp Phe Asp Asp Pro Lys Asn Thr Thr Gly Ala Leu Thr Thr
 805 810 815

Arg Leu Ala Asn Asp Ala Ala Gln Val Lys Gly Ala Ile Gly Ser Arg
 820 825 830

Leu Ala Val Ile Thr Gln Asn Ile Ala Asn Leu Gly Thr Gly Ile Ile
 835 840 845

Ile Ser Phe Ile Tyr Gly Trp Gln Leu Thr Leu Leu Leu Ala Ile
 850 855 860

Val Pro Ile Ile Ala Ile Ala Gly Val Val Glu Met Lys Met Leu Ser
 865 870 875 880

Gly Gln Ala Leu Lys Asp Lys Lys Glu Leu Glu Gly Ala Gly Lys Ile
 885 890 895

Ala Thr Glu Ala Ile Glu Asn Phe Arg Thr Val Val Ser Leu Thr Gln
 900 905 910

Glu Gln Lys Phe Glu His Met Tyr Ala Gln Ser Leu Gln Val Pro Tyr
 915 920 925

Arg Asn Ser Leu Arg Lys Ala His Ile Phe Gly Ile Thr Phe Ser Phe
 930 935 940

Thr Gln Ala Met Met Tyr Phe Ser Tyr Ala Gly Cys Phe Arg Phe Gly
 945 950 955 960

Ala Tyr Leu Val Ala His Lys Leu Met Ser Phe Glu Asp Val Leu Leu
 965 970 975

Val Phe Ser Ala Val Val Phe Gly Ala Met Ala Val Gly Gln Val Ser
 980 985 990

Ser Phe Ala Pro Asp Tyr Ala Lys Ala Lys Ile Ser Ala Ala His Ile
 995 1000 1005

Ile Met Ile Ile Glu Lys Thr Pro Leu Ile Asp Ser Tyr Ser Thr
 1010 1015 1020

Glu Gly Leu Met Pro Asn Thr Leu Glu Gly Asn Val Thr Phe Gly
 1025 1030 1035

Protein Complexes associated with APP-processing

Glu Val Val Phe Asn Tyr Pro Thr Arg Pro Asp Ile Pro Val Leu
 1040 1045 1050

Gln Gly Leu Ser Leu Glu Val Lys Lys Gly Gln Thr Leu Ala Leu
 1055 1060 1065

Val Gly Ser Ser Gly Cys Gly Lys Ser Thr Val Val Gln Leu Leu
 1070 1075 1080

Glu Arg Phe Tyr Asp Pro Leu Ala Gly Lys Val Leu Leu Asp Gly
 1085 1090 1095

Lys Glu Ile Lys Arg Leu Asn Val Gln Trp Leu Arg Ala His Leu
 1100 1105 1110

Gly Ile Val Ser Gln Glu Pro Ile Leu Phe Asp Cys Ser Ile Ala
 1115 1120 1125

Glu Asn Ile Ala Tyr Gly Asp Asn Ser Arg Val Val Ser Gln Glu
 1130 1135 1140

Glu Ile Val Arg Ala Ala Lys Glu Ala Asn Ile His Ala Phe Ile
 1145 1150 1155

Glu Ser Leu Pro Asn Lys Tyr Ser Thr Lys Val Gly Asp Lys Gly
 1160 1165 1170

Thr Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile Ala Ile Ala Arg
 1175 1180 1185

Ala Leu Val Arg Gln Pro His Ile Leu Leu Leu Asp Glu Ala Thr
 1190 1195 1200

Ser Ala Leu Asp Thr Glu Ser Glu Lys Val Val Gln Glu Ala Leu
 1205 1210 1215

Asp Lys Ala Arg Glu Gly Arg Thr Cys Ile Val Ile Ala His Arg
 1220 1225 1230

Leu Ser Thr Ile Gln Asn Ala Asp Leu Ile Val Val Phe Gln Asn
 1235 1240 1245

Gly Arg Val Lys Glu His Gly Thr His Gln Gln Leu Leu Ala Gln
 1250 1255 1260

Lys Gly Ile Tyr Phe Ser Met Val Ser Val Gln Ala Gly Thr Lys
 1265 1270 1275

Arg Gln
 1280

Protein Complexes associated with APP-processing

<210> 102

<211> 773

<212> PRT

<213> Homo sapiens

<400> 102

Met Phe Ser Leu Ser Ser Thr Val Gln Pro Gln Phe Thr Val Pro Leu
 1 5 10 15

Ser His Leu Ile Asn Ala Phe His Thr Pro Lys Asn Thr Ser Val Ser
 20 25 30

Leu Ser Gly Val Ser Val Ser Gln Asn Gln His Arg Asp Val Val Pro
 35 40 45

Glu His Glu Ala Pro Ser Ser Glu Cys Met Phe Ser Asp Phe Leu Thr
 50 55 60

Lys Leu Asn Ile Val Ser Ile Gly Lys Gly Lys Ile Phe Glu Gly Tyr
 65 70 75 80

Arg Ser Met Phe Met Glu Pro Ala Lys Arg Met Lys Lys Ser Leu Asp
 85 90 95

Thr Thr Asp Asn Trp His Ile Arg Pro Glu Pro Phe Ser Leu Ser Ile
 100 105 110

Pro Pro Ser Leu Asn Leu Arg Asp Leu Gly Leu Ser Glu Leu Lys Ile
 115 120 125

Gly Gln Ile Asp Gln Leu Val Glu Asn Leu Leu Pro Gly Phe Cys Lys
 130 135 140

Gly Lys Asn Ile Ser Ser His Trp His Thr Ser His Val Ser Ala Gln
 145 150 155 160

Ser Phe Phe Glu Asn Lys Tyr Gly Asn Leu Asp Ile Phe Ser Thr Leu
 165 170 175

Arg Ser Ser Cys Leu Tyr Arg His His Ser Arg Ala Leu Gln Ser Ile
 180 185 190

Cys Ser Asp Leu Gln Tyr Trp Pro Val Phe Ile Gln Ser Arg Gly Phe
 195 200 205

Lys Thr Leu Lys Ser Arg Thr Arg Arg Leu Gln Ser Thr Ser Glu Arg
 210 215 220

Protein Complexes associated with APP-processing
 Leu Ala Glu Thr Gln Asn Ile Ala Pro Ser Phe Val Lys Gly Phe Leu
 225 230 235 240

Leu Arg Asp Arg Gly Ser Asp Val Glu Ser Leu Asp Lys Leu Met Lys
 245 250 255

Thr Lys Asn Ile Pro Glu Ala His Gln Asp Ala Phe Lys Thr Gly Phe
 260 265 270

Ala Glu Gly Phe Leu Lys Ala Gln Ala Leu Thr Gln Lys Thr Asn Asp
 275 280 285

Ser Leu Arg Arg Thr Arg Leu Ile Leu Phe Val Leu Leu Leu Phe Gly
 290 295 300

Ile Tyr Gly Leu Leu Lys Asn Pro Phe Leu Ser Val Arg Phe Arg Thr
 305 310 315 320

Thr Thr Gly Leu Asp Ser Ala Val Asp Pro Val Gln Met Lys Asn Val
 325 330 335

Thr Phe Glu His Val Lys Gly Val Glu Glu Ala Lys Gln Glu Leu Gln
 340 345 350

Glu Val Val Glu Phe Leu Lys Asn Pro Gln Lys Phe Thr Ile Leu Gly
 355 360 365

Gly Lys Leu Pro Lys Gly Ile Leu Leu Val Gly Pro Pro Gly Thr Gly
 370 375 380

Lys Thr Leu Leu Ala Arg Ala Val Ala Gly Glu Ala Asp Val Pro Phe
 385 390 395 400

Tyr Tyr Ala Ser Gly Ser Glu Phe Asp Glu Met Phe Val Gly Val Gly
 405 410 415

Ala Ser Arg Ile Arg Asn Leu Phe Arg Glu Ala Lys Ala Asn Ala Pro
 420 425 430

Cys Val Ile Phe Ile Asp Glu Leu Asp Ser Val Gly Gly Lys Arg Ile
 435 440 445

Glu Ser Pro Met His Pro Tyr Ser Arg Gln Thr Ile Asn Gln Leu Leu
 450 455 460

Ala Glu Met Asp Gly Phe Lys Pro Asn Glu Gly Val Ile Ile Ile Gly
 465 470 475 480

Ala Thr Asn Phe Pro Glu Ala Leu Asp Asn Ala Leu Ile Arg Pro Gly
 485 490 495

Protein Complexes associated with APP-processing

Arg Phe Asp Met Gln Val Thr Val Pro Arg Pro Asp Val Lys Gly Arg
 500 505 510

Thr Glu Ile Leu Lys Trp Tyr Leu Asn Lys Ile Lys Phe Asp Gln Ser
 515 520 525

Val Asp Pro Glu Ile Ile Ala Arg Gly Thr Val Gly Phe Ser Gly Ala
 530 535 540

Glu Leu Glu Asn Leu Val Asn Gln Ala Ala Leu Lys Ala Ala Val Asp
 545 550 555 560

Gly Lys Glu Met Val Thr Met Lys Glu Leu Glu Phe Ser Lys Asp Lys
 565 570 575

Ile Leu Met Gly Pro Glu Arg Arg Ser Val Glu Ile Asp Asn Lys Asn
 580 585 590

Lys Thr Ile Thr Ala Tyr His Glu Ser Gly His Ala Ile Ile Ala Tyr
 595 600 605

Tyr Thr Lys Asp Ala Met Pro Ile Asn Lys Ala Thr Ile Met Pro Arg
 610 615 620

Gly Pro Thr Leu Gly His Val Ser Leu Leu Pro Glu Asn Asp Arg Trp
 625 630 635 640

Asn Glu Thr Arg Ala Gln Leu Leu Ala Gln Met Asp Val Ser Met Gly
 645 650 655

Gly Arg Val Ala Glu Glu Leu Ile Phe Gly Thr Asp His Ile Thr Thr
 660 665 670

Gly Ala Ser Ser Asp Phe Asp Asn Ala Thr Lys Ile Ala Lys Arg Met
 675 680 685

Val Thr Lys Phe Gly Met Ser Glu Lys Leu Gly Val Met Thr Tyr Ser
 690 695 700

Asp Thr Gly Lys Leu Ser Pro Glu Thr Gln Ser Ala Ile Glu Gln Glu
 705 710 715 720

Ile Arg Ile Leu Leu Arg Asp Ser Tyr Glu Arg Ala Lys His Ile Leu
 725 730 735

Lys Thr His Ala Lys Glu His Lys Asn Leu Ala Glu Ala Leu Leu Thr
 740 745 750

Tyr Glu Thr Leu Asp Ala Lys Glu Ile Gln Ile Val Leu Glu Gly Lys
 755 760 765

Protein Complexes associated with APP-processing
 Lys Leu Glu Val Arg
 770

<210> 103

<211> 632

<212> PRT

<213> Homo sapiens

<400> 103

Met Glu Thr Pro Ala Ala Ala Ala Pro Ala Gly Ser Leu Phe Pro Ser
 1 5 10 15

Phe Leu Leu Leu Ala Cys Gly Thr Leu Val Ala Ala Leu Leu Gly Ala
 20 25 30

Ala His Arg Leu Gly Leu Phe Tyr Gln Leu Leu His Lys Val Asp Lys
 35 40 45

Ala Ser Val Arg His Gly Gly Glu Asn Val Ala Ala Val Leu Arg Ala
 50 55 60

His Gly Val Arg Phe Ile Phe Thr Leu Val Gly Gly His Ile Ser Pro
 65 70 75 80

Leu Leu Val Ala Cys Glu Lys Leu Gly Ile Arg Val Val Asp Thr Arg
 85 90 95

His Glu Val Thr Ala Val Phe Ala Ala Asp Ala Met Ala Arg Leu Ser
 100 105 110

Gly Thr Val Gly Val Ala Ala Val Thr Ala Gly Pro Gly Leu Thr Asn
 115 120 125

Thr Val Thr Ala Val Lys Asn Ala Gln Met Ala Gln Ser Pro Ile Leu
 130 135 140

Leu Leu Gly Gly Ala Ala Ser Thr Leu Leu Gln Asn Arg Gly Ala Leu
 145 150 155 160

Gln Ala Val Asp Gln Leu Ser Leu Phe Arg Pro Leu Cys Lys Phe Cys
 165 170 175

Val Ser Val Arg Arg Val Arg Asp Ile Val Pro Thr Leu Arg Ala Ala
 180 185 190

Met Ala Ala Ala Gln Ser Gly Thr Pro Gly Pro Val Phe Val Glu Leu
 195 200 205

Protein Complexes associated with APP-processing

Pro Val Asp Val Leu Tyr Pro Tyr Phe Met Val Gln Lys Glu Met Val
 210 215 220

Pro Ala Lys Pro Pro Lys Gly Leu Val Gly Arg Val Val Ser Trp Tyr
 225 230 235 240

Leu Glu Asn Tyr Leu Ala Asn Leu Phe Ala Gly Ala Trp Glu Pro Gln
 245 250 255

Pro Glu Gly Pro Leu Pro Leu Asp Ile Pro Gln Ala Ser Pro Gln Gln
 260 265 270

Val Gln Arg Cys Val Glu Ile Leu Ser Arg Ala Lys Arg Pro Leu Met
 275 280 285

Val Leu Gly Ser Gln Ala Leu Leu Thr Pro Thr Ser Ala Asp Lys Leu
 290 295 300

Arg Ala Ala Val Glu Thr Leu Gly Val Pro Cys Phe Leu Gly Gly Met
 305 310 315 320

Ala Arg Gly Leu Leu Gly Arg Asn His Pro Leu His Ile Arg Glu Asn
 325 330 335

Arg Ser Ala Ala Leu Lys Lys Ala Asp Val Ile Val Leu Ala Gly Thr
 340 345 350

Val Cys Asp Phe Arg Leu Ser Tyr Gly Arg Val Leu Ser His Ser Ser
 355 360 365

Lys Ile Ile Ile Val Asn Arg Asn Arg Glu Glu Met Leu Leu Asn Ser
 370 375 380

Asp Ile Phe Trp Lys Pro Gln Glu Ala Val Gln Gly Asp Val Gly Ser
 385 390 395 400

Phe Val Leu Lys Leu Val Glu Gly Leu Gln Gly Gln Thr Trp Ala Pro
 405 410 415

Asp Trp Val Glu Glu Leu Arg Glu Ala Asp Arg Gln Lys Glu Gln Thr
 420 425 430

Phe Arg Glu Lys Ala Ala Met Pro Val Ala Gln His Leu Asn Pro Val
 435 440 445

Gln Val Leu Gln Leu Val Glu Glu Thr Leu Pro Asp Asn Ser Ile Leu
 450 455 460

Val Val Asp Gly Gly Asp Phe Val Gly Thr Ala Ala His Leu Val Gln
 465 470 475 480

Protein Complexes associated with APP-processing

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Protein Complexes associated with APP-processing

Ala Gly Met Asn Arg Val Phe Leu Gln Arg Leu Leu Trp Leu Leu Arg
 65 70 75 80

Leu Leu Phe Pro Arg Val Leu Cys Arg Glu Thr Gly Leu Leu Ala Leu
 85 90 95

His Ser Ala Ala Leu Val Ser Arg Thr Phe Leu Ser Val Tyr Val Ala
 100 105 110

Arg Leu Asp Gly Arg Leu Ala Arg Cys Ile Ala Arg Lys Asp Pro Arg
 115 120 125

Ala Phe Gly Trp Gln Leu Leu Gln Trp Leu Leu Ile Ala Leu Pro Ala
 130 135 140

Thr Phe Val Asn Ser Ala Ile Arg Tyr Leu Glu Gly Gln Leu Ala Leu
 145 150 155 160

Ser Phe Arg Ser Arg Leu Val Ala His Ala Tyr Arg Leu Tyr Phe Ser
 165 170 175

Gln Gln Thr Tyr Tyr Arg Val Ser Asn Met Asp Gly Arg Leu Arg Asn
 180 185 190

Pro Asp Gln Ser Leu Thr Glu Asp Val Val Ala Phe Ala Ala Ser Val
 195 200 205

Ala His Leu Tyr Ser Asn Leu Thr Lys Pro Leu Leu Asp Val Ala Val
 210 215 220

Thr Ser Tyr Thr Leu Leu Arg Ala Ala Arg Ser Arg Gly Ala Gly Thr
 225 230 235 240

Ala Trp Pro Ser Ala Ile Ala Gly Leu Val Val Phe Leu Thr Ala Asn
 245 250 255

Val Leu Arg Ala Phe Ser Pro Lys Phe Gly Glu Leu Val Ala Glu Glu
 260 265 270

Ala Arg Arg Lys Gly Glu Leu Arg Tyr Met His Ser Arg Val Val Ala
 275 280 285

Asn Ser Glu Glu Ile Ala Phe Tyr Gly Gly His Glu Val Glu Leu Ala
 290 295 300

Leu Leu Gln Arg Ser Tyr Gln Asp Leu Ala Ser Gln Ile Asn Leu Ile
 305 310 315 320

Leu Leu Glu Arg Leu Trp Tyr Val Met Leu Glu Gln Phe Leu Met Lys
 325 330 335

Protein Complexes associated with APP-processing

Tyr Val Trp Ser Ala Ser Gly Leu Leu Met Val Ala Val Pro Ile Ile
 340 345 350

Thr Ala Thr Gly Tyr Ser Glu Ser Asp Ala Glu Ala Val Lys Lys Ala
 355 360 365

Ala Leu Glu Lys Lys Glu Glu Glu Leu Val Ser Glu Arg Thr Glu Ala
 370 375 380

Phe Thr Ile Ala Arg Asn Leu Leu Thr Ala Ala Ala Asp Ala Ile Glu
 385 390 395 400

Arg Ile Met Ser Ser Tyr Lys Glu Val Thr Glu Leu Ala Gly Tyr Thr
 405 410 415

Ala Arg Val His Glu Met Phe Gln Val Phe Glu Asp Val Gln Arg Cys
 420 425 430

His Phe Lys Arg Pro Arg Glu Leu Glu Asp Ala Gln Ala Gly Ser Gly
 435 440 445

Thr Ile Gly Arg Ser Gly Val Arg Val Glu Gly Pro Leu Lys Ile Arg
 450 455 460

Gly Gln Val Val Asp Val Glu Gln Gly Ile Ile Cys Glu Asn Ile Pro
 465 470 475 480

Ile Val Thr Pro Ser Gly Glu Val Val Val Ala Ser Leu Asn Ile Arg
 485 490 495

Val Glu Glu Gly Met His Leu Leu Ile Thr Gly Pro Asn Gly Cys Gly
 500 505 510

Lys Ser Ser Leu Phe Arg Ile Leu Gly Gly Leu Trp Pro Thr Tyr Gly
 515 520 525

Gly Val Leu Tyr Lys Pro Pro Pro Gln Arg Met Phe Tyr Ile Pro Gln
 530 535 540

Arg Pro Tyr Met Ser Val Gly Ser Leu Arg Asp Gln Val Ile Tyr Pro
 545 550 555 560

Asp Ser Val Glu Asp Met Gln Arg Lys Gly Tyr Ser Glu Gln Asp Leu
 565 570 575

Glu Ala Ile Leu Asp Val Val His Leu His His Ile Leu Gln Arg Glu
 580 585 590

Gly Gly Trp Glu Ala Met Cys Asp Trp Lys Asp Val Leu Ser Gly Gly
 595 600 605

Protein Complexes associated with APP-processing

Glu Lys Gln Arg Ile Gly Met Ala Arg Met Phe Tyr His Arg Pro Lys
 610 615 620

Tyr Ala Leu Leu Asp Glu Cys Thr Ser Ala Val Ser Ile Asp Val Glu
 625 630 635 640

Gly Lys Ile Phe Gln Ala Ala Lys Asp Ala Gly Ile Ala Leu Leu Ser
 645 650 655

Ile Thr His Arg Pro Ser Leu Trp Lys Tyr His Thr His Leu Leu Gln
 660 665 670

Phe Asp Gly Glu Gly Gly Trp Lys Phe Glu Lys Leu Asp Ser Ala Ala
 675 680 685

Arg Leu Ser Leu Thr Glu Glu Lys Gln Arg Leu Glu Gln Gln Leu Ala
 690 695 700

Gly Ile Pro Lys Met Gln Arg Arg Leu Gln Glu Leu Cys Gln Ile Leu
 705 710 715 720

Gly Glu Ala Val Ala Pro Ala His Val Pro Ala Pro Ser Pro Gln Gly
 725 730 735

Pro Gly Gly Leu Gln Gly Ala Ser Thr
 740 745

<210> 105
 <211> 469
 <212> PRT
 <213> Homo sapiens

<400> 105

Met Gly Thr Val His Ala Arg Ser Leu Glu Pro Leu Pro Ser Ser Gly
 1 5 10 15

Pro Asp Phe Gly Gly Leu Gly Glu Glu Ala Glu Phe Val Glu Val Glu
 20 25 30

Pro Glu Ala Lys Gln Glu Ile Leu Glu Asn Lys Asp Val Val Val Gln
 35 40 45

His Val His Phe Asp Gly Leu Gly Arg Thr Lys Asp Asp Ile Ile Ile
 50 55 60

Cys Glu Ile Gly Asp Val Phe Lys Ala Lys Asn Leu Ile Glu Val Met
 65 70 75 80

Protein Complexes associated with APP-processing

Arg Lys Ser His Glu Ala Arg Glu Lys Leu Leu Arg Leu Gly Ile Phe
85 90 95

Arg Gln Val Asp Val Leu Ile Asp Thr Cys Gln Gly Asp Asp Ala Leu
100 105 110

Pro Asn Gly Leu Asp Val Thr Phe Glu Val Thr Glu Leu Arg Arg Leu
115 120 125

Thr Gly Ser Tyr Asn Thr Met Val Gly Asn Asn Glu Gly Ser Met Val
130 135 140

Leu Gly Leu Lys Leu Pro Asn Leu Leu Gly Arg Ala Glu Lys Val Thr
145 150 155 160

Phe Gln Phe Ser Tyr Gly Thr Lys Glu Thr Ser Tyr Gly Leu Ser Phe
165 170 175

Phe Lys Pro Arg Pro Gly Asn Phe Glu Arg Asn Phe Ser Val Asn Leu
180 185 190

Tyr Lys Val Thr Gly Gln Phe Pro Trp Ser Ser Leu Arg Glu Thr Asp
195 200 205

Arg Gly Met Ser Ala Glu Tyr Ser Phe Pro Ile Trp Lys Thr Ser His
210 215 220

Thr Val Lys Trp Glu Gly Val Trp Arg Glu Leu Gly Cys Leu Ser Arg
225 230 235 240

Thr Ala Ser Phe Ala Val Arg Lys Glu Ser Gly His Ser Leu Lys Ser
245 250 255

Ser Leu Ser His Ala Met Val Ile Asp Ser Arg Asn Ser Ser Ile Leu
260 265 270

Pro Arg Arg Gly Ala Leu Leu Lys Val Asn Gln Glu Leu Ala Gly Tyr
275 280 285

Thr Gly Gly Asp Val Ser Phe Ile Lys Glu Asp Phe Glu Leu Gln Leu
290 295 300

Asn Lys Gln Leu Ile Phe Asp Ser Val Phe Ser Ala Ser Phe Trp Gly
305 310 315 320

Gly Met Leu Val Pro Ile Gly Asp Lys Pro Ser Ser Ile Ala Asp Arg
325 330 335

Phe Tyr Leu Gly Gly Pro Thr Ser Val Arg Gly Phe Ser Met His Ser
340 345 350

Protein Complexes associated with APP-processing
 Ile Gly Pro Gln Ser Glu Gly Asp Tyr Leu Gly Gly Glu Ala Tyr Trp
 355 360 365

Ala Gly Gly Leu His Leu Tyr Thr Pro Leu Pro Phe Arg Pro Gly Gln
 370 375 380

Gly Gly Phe Gly Glu Leu Phe Arg Thr His Phe Phe Leu Asn Ala Gly
 385 390 395 400

Asn Leu Cys Asn Leu Asn Tyr Gly Glu Gly Pro Lys Ala His Ile Arg
 405 410 415

Lys Leu Ala Glu Cys Ile Arg Trp Ser Tyr Gly Ala Gly Ile Val Leu
 420 425 430

Arg Leu Gly Asn Ile Ala Arg Leu Glu Leu Asn Tyr Cys Val Pro Met
 435 440 445

Gly Val Gln Thr Gly Asp Arg Ile Cys Asp Gly Val Gln Phe Gly Ala
 450 455 460

Gly Ile Arg Phe Leu
 465

<210> 106

<211> 194

<212> PRT

<213> Homo sapiens

<400> 106

Gly Ser Arg Ala Ser Thr Leu Leu Arg Asp Glu Glu Leu Glu Glu Ile
 1 5 10 15

Lys Lys Glu Thr Gly Phe Ser His Ser Gln Ile Thr Arg Leu Tyr Ser
 20 25 30

Arg Phe Thr Ser Leu Asp Lys Gly Glu Asn Gly Thr Leu Ser Arg Glu
 35 40 45

Asp Phe Gln Arg Ile Pro Glu Leu Ala Ile Asn Pro Leu Gly Asp Arg
 50 55 60

Ile Ile Asn Ala Phe Phe Pro Glu Gly Glu Asp Gln Val Asn Phe Arg
 65 70 75 80

Gly Phe Met Arg Thr Leu Ala His Phe Arg Pro Ile Glu Asp Asn Glu
 85 90 95

Protein Complexes associated with APP-processing
 Lys Ser Lys Asp Val Asn Gly Pro Glu Pro Leu Asn Ser Arg Ser Asn
 100 105 110

Lys Leu His Phe Ala Phe Arg Leu Tyr Asp Leu Asp Lys Asp Glu Lys
 115 120 125

Ile Ser Arg Asp Glu Leu Leu Gln Val Leu Arg Met Met Val Gly Val
 130 135 140

Asn Ile Ser Asp Glu Gln Leu Gly Ser Ile Ala Asp Arg Thr Ile Gln
 145 150 155 160

Glu Ala Asp Gln Asp Gly Asp Ser Ala Ile Ser Phe Thr Glu Phe Val
 165 170 175

Lys Val Leu Glu Lys Val Asp Val Glu Gln Lys Met Ser Ile Arg Phe
 180 185 190

Leu His

<210> 107

<211> 914

<212> PRT

<213> Homo sapiens

<400> 107

Met Ala Ser Glu Ser Ser Pro Leu Leu Ala Tyr Arg Leu Leu Gly Glu
 1 5 10 15

Glu Gly Val Ala Leu Pro Ala Asn Gly Ala Gly Gly Pro Gly Gly Ala
 20 25 30

Ser Ala Arg Lys Leu Ser Thr Phe Leu Gly Val Val Val Pro Thr Val
 35 40 45

Leu Ser Met Phe Ser Ile Val Val Phe Leu Arg Ile Gly Phe Val Val
 50 55 60

Gly His Ala Gly Leu Leu Gln Ala Leu Ala Met Leu Leu Val Ala Tyr
 65 70 75 80

Phe Ile Leu Ala Leu Thr Val Leu Ser Val Cys Ala Ile Ala Thr Asn
 85 90 95

Gly Ala Val Gln Gly Gly Gly Ala Tyr Phe Met Ile Ser Arg Thr Leu
 100 105 110

Protein Complexes associated with APP-processing
 Gly Pro Glu Val Gly Gly Ser Ile Gly Leu Met Phe Tyr Leu Ala Asn
 115 120 125

Val Cys Gly Cys Ala Val Ser Leu Leu Gly Leu Val Glu Ser Val Leu
 130 135 140

Asp Val Phe Gly Ala Asp Ala Thr Gly Pro Ser Gly Leu Arg Val Leu
 145 150 155 160

Pro Gln Gly Tyr Gly Trp Asn Leu Leu Tyr Gly Ser Leu Leu Leu Gly
 165 170 175

Leu Val Gly Gly Val Cys Thr Leu Gly Ala Gly Leu Tyr Ala Arg Ala
 180 185 190

Ser Phe Leu Thr Phe Leu Leu Val Ser Gly Ser Leu Ala Ser Val Leu
 195 200 205

Ile Ser Phe Val Ala Val Gly Pro Arg Asp Ile Arg Leu Thr Pro Arg
 210 215 220

Pro Gly Pro Asn Gly Ser Ser Leu Pro Pro Arg Phe Gly His Phe Thr
 225 230 235 240

Gly Phe Asn Ser Ser Thr Leu Lys Asp Asn Leu Gly Ala Gly Tyr Ala
 245 250 255

Glu Asp Tyr Thr Thr Gly Ala Val Met Asn Phe Ala Asn Val Phe Ala
 260 265 270

Val Leu Phe Asn Gly Cys Thr Gly Ile Met Ala Gly Ala Asn Met Ser
 275 280 285

Gly Glu Leu Lys Asp Pro Ser Arg Ala Ile Pro Leu Gly Thr Ile Val
 290 295 300

Ala Val Ala Tyr Thr Phe Phe Val Tyr Val Leu Leu Phe Phe Leu Ser
 305 310 315 320

Ser Phe Thr Cys Asp Arg Thr Leu Leu Gln Glu Asp Tyr Gly Phe Phe
 325 330 335

Arg Ala Ile Ser Leu Trp Pro Pro Leu Val Leu Ile Gly Ile Tyr Ala
 340 345 350

Thr Ala Leu Ser Ala Ser Met Ser Ser Leu Ile Gly Ala Ser Arg Ile
 355 360 365

Leu His Ala Leu Ala Arg Asp Asp Leu Phe Gly Val Ile Leu Ala Pro
 370 375 380

Protein Complexes associated with APP-processing
 Ala Lys Val Val Ser Arg Gly Gly Asn Pro Trp Ala Ala Val Leu Tyr
 385 390 395 400

Ser Trp Gly Leu Val Gln Leu Val Leu Leu Ala Gly Lys Leu Asn Thr
 405 410 415

Leu Ala Ala Val Val Thr Val Phe Tyr Leu Val Ala Tyr Ala Ala Val
 420 425 430

Asp Leu Ser Cys Leu Ser Leu Glu Trp Ala Ser Ala Pro Asn Phe Arg
 435 440 445

Pro Thr Phe Ser Leu Phe Ser Trp His Thr Cys Leu Leu Gly Val Ala
 450 455 460

Ser Cys Leu Leu Met Met Phe Leu Ile Ser Pro Gly Ala Ala Gly Gly
 465 470 475 480

Ser Leu Leu Leu Met Gly Leu Leu Ala Ala Leu Leu Thr Ala Arg Gly
 485 490 495

Gly Pro Ser Ser Trp Gly Tyr Val Ser Gln Ala Leu Leu Phe His Gln
 500 505 510

Val Arg Lys Tyr Leu Leu Arg Leu Asp Val Arg Lys Asp His Val Lys
 515 520 525

Phe Trp Arg Pro Gln Leu Leu Leu Leu Val Gly Asn Pro Arg Gly Ala
 530 535 540

Leu Pro Leu Leu Arg Leu Ala Asn Gln Leu Lys Lys Gly Gly Leu Tyr
 545 550 555 560

Val Leu Gly His Val Thr Leu Gly Asp Leu Asp Ser Leu Pro Ser Asp
 565 570 575

Pro Val Gln Pro Gln Tyr Gly Ala Trp Leu Ser Leu Val Asp Arg Ala
 580 585 590

Gln Val Lys Ala Phe Val Asp Leu Thr Phe Ser Pro Ser Val Arg Gln
 595 600 605

Gly Ala Gln His Leu Leu Arg Ile Ser Gly Leu Gly Gly Met Lys Pro
 610 615 620

Asn Thr Leu Val Leu Gly Phe Tyr Asp Asp Ala Pro Pro Gln Asp His
 625 630 635 640

Phe Leu Thr Asp Pro Ala Phe Ser Glu Pro Ala Asp Ser Thr Arg Glu
 645 650 655

Protein Complexes associated with APP-processing

Gly Ser Ser Pro Ala Leu Ser Thr Leu Phe Pro Pro Pro Arg Ala Pro
 660 665 670

Gly Ser Pro Arg Ala Leu Asn Pro Gln Asp Tyr Val Ala Thr Val Ala
 675 680 685

Asp Ala Leu Lys Met Asn Lys Asn Val Val Leu Ala Arg Ala Ser Gly
 690 695 700

Ala Leu Pro Pro Glu Arg Leu Ser Arg Gly Ser Gly Gly Thr Ser Gln
 705 710 715 720

Leu His His Val Asp Val Trp Pro Leu Asn Leu Leu Arg Pro Arg Gly
 725 730 735

Gly Pro Gly Tyr Val Asp Val Cys Gly Leu Phe Leu Leu Gln Met Ala
 740 745 750

Thr Ile Leu Gly Met Val Pro Ala Trp His Ser Ala Arg Leu Arg Ile
 755 760 765

Phe Leu Cys Leu Gly Pro Arg Glu Ala Pro Gly Ala Ala Glu Gly Arg
 770 775 780

Leu Arg Ala Leu Leu Ser Gln Leu Arg Ile Arg Ala Glu Val Gln Glu
 785 790 795 800

Val Val Trp Gly Glu Gly Ala Gly Ala Gly Glu Pro Glu Ala Glu Glu
 805 810 815

Glu Gly Asp Phe Val Asn Ser Gly Arg Gly Asp Ala Glu Ala Glu Ala
 820 825 830

Leu Ala Arg Ser Ala Asn Ala Leu Val Arg Ala Gln Gln Gly Arg Gly
 835 840 845

Thr Gly Gly Gly Pro Gly Gly Pro Glu Gly Gly Asp Ala Glu Gly Pro
 850 855 860

Ile Thr Ala Leu Thr Phe Leu Tyr Leu Pro Arg Pro Pro Ala Asp Pro
 865 870 875 880

Ala Arg Tyr Pro Arg Tyr Leu Ala Leu Leu Glu Thr Leu Thr Arg Asp
 885 890 895

Leu Gly Pro Thr Leu Leu Val His Gly Val Thr Pro Val Thr Cys Thr
 900 905 910

Asp Leu

Protein Complexes associated with APP-processing

<210> 108

<211> 779

<212> PRT

<213> Homo sapiens

<400> 108

Met Ala Ser Phe Val Thr Glu Val Leu Ala His Ser Gly Arg Leu Glu
 1 5 10 15

Lys Glu Asp Leu Gly Thr Arg Ile Ser Arg Leu Thr Arg Arg Val Glu
 20 25 30

Glu Ile Lys Gly Glu Val Cys Asn Met Ile Ser Lys Lys Tyr Ser Glu
 35 40 45

Phe Leu Pro Ser Met Gln Ser Ala Gln Gly Leu Ile Thr Gln Val Asp
 50 55 60

Lys Leu Ser Glu Asp Ile Asp Leu Leu Lys Ser Arg Ile Glu Ser Glu
 65 70 75 80

Val Arg Arg Asp Leu His Val Ser Thr Gly Glu Phe Thr Asp Leu Lys
 85 90 95

Gln Gln Leu Glu Arg Asp Ser Val Val Leu Ser Leu Leu Lys Gln Leu
 100 105 110

Gln Glu Phe Ser Thr Ala Ile Glu Glu Tyr Asn Cys Ala Leu Thr Glu
 115 120 125

Lys Lys Tyr Val Thr Gly Ala Gln Arg Leu Glu Glu Ala Gln Lys Cys
 130 135 140

Leu Lys Leu Leu Lys Ser Arg Lys Cys Phe Asp Leu Lys Ile Leu Lys
 145 150 155 160

Ser Leu Ser Met Glu Leu Thr Ile Gln Lys Gln Asn Ile Leu Tyr His
 165 170 175

Leu Gly Glu Glu Trp Gln Lys Leu Ile Val Trp Lys Phe Pro Pro Ser
 180 185 190

Lys Asp Thr Ser Ser Leu Glu Ser Tyr Leu Gln Thr Glu Leu His Leu
 195 200 205

Tyr Thr Glu Gln Ser His Lys Glu Glu Lys Thr Pro Met Pro Pro Ile
 210 215 220

Protein Complexes associated with APP-processing

Ser Ser Val Leu Leu Ala Phe Ser Val Leu Gly Glu Leu His Ser Lys
 225 230 235 240

Leu Lys Ser Phe Gly Gln Met Leu Leu Lys Tyr Ile Leu Arg Pro Leu
 245 250 255

Ala Ser Cys Pro Ser Leu His Ala Val Ile Glu Ser Gln Pro Asn Ile
 260 265 270

Val Ile Ile Arg Phe Glu Ser Ile Met Thr Asn Leu Glu Tyr Pro Ser
 275 280 285

Pro Ser Glu Val Phe Thr Lys Ile Arg Leu Val Leu Glu Val Leu Gln
 290 295 300

Lys Gln Leu Leu Asp Leu Pro Leu Asp Thr Asp Leu Glu Asn Glu Lys
 305 310 315 320

Thr Ser Thr Val Pro Leu Ala Glu Met Leu Gly Asp Met Ile Trp Glu
 325 330 335

Asp Leu Ser Glu Cys Leu Ile Lys Asn Cys Leu Val Tyr Ser Ile Pro
 340 345 350

Thr Asn Ser Ser Lys Leu Gln Gln Tyr Glu Glu Ile Ile Gln Ser Thr
 355 360 365

Glu Glu Phe Glu Asn Ala Leu Lys Glu Met Arg Phe Leu Lys Gly Asp
 370 375 380

Thr Thr Asp Leu Leu Lys Tyr Ala Arg Asn Ile Asn Ser His Phe Ala
 385 390 395 400

Asn Lys Lys Cys Gln Asp Val Ile Val Ala Ala Arg Asn Leu Met Thr
 405 410 415

Ser Glu Ile His Asn Thr Val Lys Ile Ile Pro Asp Ser Lys Ile Asn
 420 425 430

Val Pro Glu Leu Pro Thr Pro Asp Glu Asp Asn Lys Leu Glu Val Gln
 435 440 445

Lys Val Ser Asn Thr Gln Tyr His Glu Val Met Asn Leu Glu Pro Glu
 450 455 460

Asn Thr Leu Asp Gln His Ser Phe Ser Leu Pro Thr Cys Arg Ile Ser
 465 470 475 480

Glu Ser Val Lys Lys Leu Met Glu Leu Ala Tyr Gln Thr Leu Leu Glu
 485 490 495

Protein Complexes associated with APP-processing

Ala Thr Thr Ser Ser Asp Gln Cys Ala Val Gln Leu Phe Tyr Ser Val
500 505 510

Arg Asn Ile Phe His Leu Phe His Asp Val Val Pro Thr Tyr His Lys
515 520 525

Glu Asn Leu Gln Lys Leu Pro Gln Leu Ala Ala Ile His His Asn Asn
530 535 540

Cys Met Tyr Ile Ala His His Leu Leu Thr Leu Gly His Gln Phe Arg
545 550 555 560

Leu Arg Leu Ala Pro Ile Leu Cys Asp Gly Thr Ala Thr Phe Val Asp
565 570 575

Leu Val Pro Gly Phe Arg Arg Leu Gly Thr Glu Cys Phe Leu Ala Gln
580 585 590

Met Arg Ala Gln Lys Gly Glu Leu Leu Glu Arg Leu Ser Ser Ala Arg
595 600 605

Asn Phe Ser Asn Met Asp Asp Glu Glu Asn Tyr Ser Ala Ala Ser Lys
610 615 620

Ala Val Arg Gln Val Leu His Gln Leu Lys Arg Leu Gly Ile Val Trp
625 630 635 640

Gln Asp Val Leu Pro Val Asn Ile Tyr Cys Lys Ala Met Gly Thr Leu
645 650 655

Leu Asn Thr Ala Ile Ser Glu Val Ile Gly Lys Ile Thr Ala Leu Glu
660 665 670

Asp Ile Ser Thr Glu Asp Gly Asp Arg Leu Tyr Ser Leu Cys Lys Thr
675 680 685

Val Met Asp Glu Gly Pro Gln Val Phe Ala Pro Leu Ser Glu Glu Ser
690 695 700

Lys Asn Lys Lys Tyr Gln Glu Glu Val Pro Val Tyr Val Pro Lys Trp
705 710 715 720

Met Pro Phe Lys Glu Leu Met Met Met Leu Gln Ala Ser Leu Gln Glu
725 730 735

Ile Gly Asp Arg Trp Ala Asp Gly Lys Gly Pro Leu Ala Ala Ala Phe
740 745 750

Ser Ser Ser Glu Val Lys Ala Leu Ile Arg Ala Leu Phe Gln Asn Thr
755 760 765

Protein Complexes associated with APP-processing

Glu Arg Arg Ala Ala Ala Leu Ala Lys Ile Lys
 770 775

<210> 109

<211> 470

<212> PRT

<213> Homo sapiens

<400> 109

Met Ser Arg Leu Gly Ala Leu Gly Gly Ala Arg Ala Gly Leu Gly Leu
 1 5 10 15

Leu Leu Gly Thr Ala Ala Gly Leu Gly Phe Leu Cys Leu Leu Tyr Ser
 20 25 30

Gln Arg Trp Lys Arg Thr Gln Arg His Gly Arg Ser Gln Ser Leu Pro
 35 40 45

Asn Ser Leu Asp Tyr Thr Gln Thr Ser Asp Pro Gly Arg His Val Met
 50 55 60

Leu Leu Arg Ala Val Pro Gly Gly Ala Gly Asp Ala Ser Val Leu Pro
 65 70 75 80

Ser Leu Pro Arg Glu Gly Gln Glu Lys Val Leu Asp Arg Leu Asp Phe
 85 90 95

Val Leu Thr Ser Leu Val Ala Leu Arg Arg Glu Val Glu Glu Leu Arg
 100 105 110

Ser Ser Leu Arg Gly Leu Ala Gly Glu Ile Val Gly Glu Val Arg Cys
 115 120 125

His Met Glu Glu Asn Gln Arg Val Ala Arg Arg Arg Arg Phe Pro Phe
 130 135 140

Val Arg Glu Arg Ser Asp Ser Thr Gly Ser Ser Ser Val Tyr Phe Thr
 145 150 155 160

Ala Ser Ser Gly Ala Thr Phe Thr Asp Ala Glu Ser Glu Gly Gly Tyr
 165 170 175

Thr Thr Ala Asn Ala Glu Ser Asp Asn Glu Arg Asp Ser Asp Lys Glu
 180 185 190

Ser Glu Asp Gly Glu Asp Glu Val Ser Cys Glu Thr Val Lys Met Gly
 195 200 205

Protein Complexes associated with APP-processing

Arg Lys Asp Ser Leu Asp Leu Glu Glu Glu Ala Ala Ser Gly Ala Ser
 210 215 220

Ser Ala Leu Glu Ala Gly Gly Ser Ser Gly Leu Glu Asp Val Leu Pro
 225 230 235 240

Leu Leu Gln Gln Ala Asp Glu Leu His Arg Gly Asp Glu Gln Gly Lys
 245 250 255

Arg Glu Gly Phe Gln Leu Leu Leu Asn Asn Lys Leu Val Tyr Gly Ser
 260 265 270

Arg Gln Asp Phe Leu Trp Arg Leu Ala Arg Ala Tyr Ser Asp Met Cys
 275 280 285

Glu Leu Thr Glu Glu Val Ser Glu Lys Lys Ser Tyr Ala Leu Asp Gly
 290 295 300

Lys Glu Glu Ala Glu Ala Ala Leu Glu Lys Gly Asp Glu Ser Ala Asp
 305 310 315 320

Cys His Leu Trp Tyr Ala Val Leu Cys Gly Gln Leu Ala Glu His Glu
 325 330 335

Ser Ile Gln Arg Arg Ile Gln Ser Gly Phe Ser Phe Lys Glu His Val
 340 345 350

Asp Lys Ala Ile Ala Leu Gln Pro Glu Asn Pro Met Ala His Phe Leu
 355 360 365

Leu Gly Arg Trp Cys Tyr Gln Val Ser His Leu Ser Trp Leu Glu Lys
 370 375 380

Lys Thr Ala Thr Ala Leu Leu Glu Ser Pro Leu Ser Ala Thr Val Glu
 385 390 395 400

Asp Ala Leu Gln Ser Phe Leu Lys Ala Glu Glu Leu Gln Pro Gly Phe
 405 410 415

Ser Lys Ala Gly Arg Val Tyr Ile Ser Lys Cys Tyr Arg Glu Leu Gly
 420 425 430

Lys Asn Ser Glu Ala Arg Trp Trp Met Lys Leu Ala Leu Glu Leu Pro
 435 440 445

Asp Val Thr Lys Glu Asp Leu Ala Ile Gln Lys Asp Leu Glu Glu Leu
 450 455 460

Glu Val Ile Leu Arg Asp
 465 470

Protein Complexes associated with APP-processing

<210> 110

<211> 195

<212> PRT

<213> Homo sapiens

<400> 110

Met Glu Asn His Lys Ser Asn Asn Lys Glu Asn Ile Thr Ile Val Asp
 1 5 10 15

Ile Ser Arg Lys Ile Asn Gln Leu Pro Glu Ala Glu Arg Asn Leu Leu
 20 25 30

Glu Asn Gly Ser Val Tyr Val Gly Leu Asn Ala Ala Leu Cys Gly Leu
 35 40 45

Ile Ala Asn Ser Leu Phe Arg Arg Ile Leu Asn Val Thr Lys Ala Arg
 50 55 60

Ile Ala Ala Gly Leu Pro Met Ala Gly Ile Pro Phe Leu Thr Thr Asp
 65 70 75 80

Leu Thr Tyr Arg Cys Phe Val Ser Phe Pro Leu Asn Thr Gly Asp Leu
 85 90 95

Asp Cys Glu Thr Cys Thr Ile Thr Arg Ser Gly Leu Thr Gly Leu Val
 100 105 110

Ile Gly Gly Leu Tyr Pro Val Phe Leu Ala Ile Pro Val Asn Gly Gly
 115 120 125

Leu Ala Ala Arg Tyr Gln Ser Ala Leu Leu Pro His Lys Gly Asn Ile
 130 135 140

Leu Ser Tyr Trp Ile Arg Thr Ser Lys Pro Val Phe Arg Lys Met Leu
 145 150 155 160

Phe Pro Ile Leu Leu Gln Thr Met Phe Ser Ala Tyr Leu Gly Ser Glu
 165 170 175

Gln Tyr Lys Leu Leu Ile Lys Ala Leu Gln Leu Ser Glu Pro Gly Lys
 180 185 190

Glu Ile His
 195

<210> 111

<211> 1907

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 111

Asp Leu Arg Arg Gln Leu Leu Ser Gly His Leu Thr Gln Asp Gln Val
 1 5 10 15

Arg Glu Val Lys Arg His Ile Thr Val Arg Leu Asp Trp Gly Asn Glu
 20 25 30

His Leu Gly Leu Asp Leu Val Pro Arg Lys Asp Phe Glu Val Val Asp
 35 40 45

Ser Asp Gln Ile Ser Val Ser Asp Leu Tyr Lys Met His Leu Ser Ser
 50 55 60

Arg Gln Ser Val Gln Gln Ser Thr Ser Gln Val Asp Thr Met Arg Pro
 65 70 75 80

Arg His Gly Glu Thr Cys Arg Met Pro Val Pro His His Phe Phe Leu
 85 90 95

Ser Leu Lys Ser Phe Thr Tyr Asn Thr Ile Gly Glu Asp Thr Asp Val
 100 105 110

Phe Phe Ser Leu Tyr Asp Met Arg Glu Gly Lys Gln Ile Ser Glu Arg
 115 120 125

Phe Leu Val Arg Leu Asn Lys Asn Gly Gly Pro Arg Asn Pro Glu Lys
 130 135 140

Ile Glu Arg Met Cys Ala Leu Phe Thr Asp Leu Ser Ser Lys Asp Met
 145 150 155 160

Lys Arg Asp Leu Tyr Ile Val Ala His Val Ile Arg Ile Gly Arg Met
 165 170 175

Leu Leu Asn Asp Ser Lys Lys Gly Pro Pro His Leu His Tyr Arg Arg
 180 185 190

Pro Tyr Gly Cys Ala Val Leu Ser Ile Leu Asp Val Leu Gln Ser Leu
 195 200 205

Thr Glu Val Lys Glu Glu Lys Asp Phe Val Leu Lys Val Tyr Thr Cys
 210 215 220

Asn Asn Glu Ser Glu Trp Ser Gln Ile His Glu Asn Ile Ile Arg Lys
 225 230 235 240

Protein Complexes associated with APP-processing

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Protein Complexes associated with APP-processing

Glu Ile Val Lys Phe Leu Gln Asp Ile Leu Asp Thr Leu Phe Val Ile
515 520 525

Leu Asp Asp Asn Thr Glu Lys Tyr Gly Leu Leu Val Phe Gln Ser Leu
530 535 540

Val Phe Ile Ile Asn Leu Leu Arg Asp Ile Lys Tyr Phe His Phe Arg
545 550 555 560

Pro Val Met Asp Thr Tyr Ile Gln Lys His Phe Ala Gly Ala Leu Ala
565 570 575

Tyr Lys Glu Leu Ile Arg Cys Leu Lys Trp Tyr Met Asp Cys Ser Ala
580 585 590

Glu Leu Ile Arg Gln Asp His Ile Gln Glu Ala Met Arg Ala Leu Glu
595 600 605

Tyr Leu Phe Lys Phe Ile Val Gln Ser Arg Ile Leu Tyr Ser Arg Ala
610 615 620

Thr Cys Gly Met Glu Glu Glu Gln Phe Arg Ser Ser Ile Gln Glu Leu
625 630 635 640

Phe Gln Ser Ile Arg Phe Val Leu Ser Leu Asp Ser Arg Asn Ser Glu
645 650 655

Thr Leu Leu Phe Thr Gln Ala Ala Leu Leu Asn Ser Phe Pro Thr Ile
660 665 670

Phe Asp Glu Leu Leu Gln Met Phe Thr Val Gln Glu Val Ala Glu Phe
675 680 685

Val Arg Gly Thr Leu Gly Ser Met Pro Ser Thr Val His Ile Gly Gln
690 695 700

Ser Met Asp Val Val Lys Leu Gln Ser Ile Ala Arg Thr Val Asp Ser
705 710 715 720

Arg Leu Phe Ser Phe Ser Glu Ser Arg Arg Ile Leu Leu Pro Val Val
725 730 735

Leu His His Ile His Leu His Leu Arg Gln Gln Lys Glu Leu Leu Ile
740 745 750

Cys Ser Gly Ile Leu Gly Ser Ile Phe Ser Ile Val Lys Thr Ser Ser
755 760 765

Leu Glu Ala Asp Val Met Glu Glu Val Glu Met Met Val Glu Ser Leu
770 775 780

Protein Complexes associated with APP-processing

Leu Asp Val Leu Leu Gln Thr Leu Leu Thr Ile Met Ser Lys Ser His
 785 790 795 800

Ala Gln Glu Ala Val Arg Gly Gln Arg Cys Pro Gln Cys Thr Ala Glu
 805 810 815

Ile Thr Gly Glu Tyr Val Ser Cys Leu Leu Ser Leu Leu Arg Gln Met
 820 825 830

Cys Asp Thr His Phe Gln His Leu Leu Asp Asn Phe Gln Ser Lys Asp
 835 840 845

Glu Leu Lys Glu Phe Leu Leu Lys Ile Phe Cys Val Phe Arg Asn Leu
 850 855 860

Met Lys Met Ser Val Phe Pro Arg Asp Trp Met Val Met Arg Leu Leu
 865 870 875 880

Thr Ser Asn Ile Ile Val Thr Thr Val Gln Tyr Leu Ser Ser Ala Leu
 885 890 895

His Lys Asn Phe Thr Glu Thr Asp Phe Asp Phe Lys Val Trp Asn Ser
 900 905 910

Tyr Phe Ser Leu Ala Val Leu Phe Ile Asn Gln Pro Ser Leu Gln Leu
 915 920 925

Glu Ile Ile Thr Ser Ala Lys Arg Lys Lys Ile Leu Asp Lys Tyr Gly
 930 935 940

Asp Met Arg Val Met Met Ala Tyr Glu Leu Phe Ser Met Trp Gln Asn
 945 950 955 960

Leu Gly Glu His Lys Ile His Phe Ile Pro Gly Met Ile Gly Pro Phe
 965 970 975

Leu Gly Val Thr Leu Val Pro Gln Pro Glu Val Arg Asn Ile Met Ile
 980 985 990

Pro Ile Phe His Asp Met Met Asp Trp Glu Gln Arg Lys Asn Gly Asn
 995 1000 1005

Phe Lys Gln Val Glu Ala Glu Leu Ile Asp Lys Leu Asp Ser Met
 1010 1015 1020

Val Ser Glu Gly Lys Gly Asp Glu Ser Tyr Arg Glu Leu Phe Ser
 1025 1030 1035

Leu Leu Thr Gln Leu Phe Gly Pro Tyr Pro Ser Leu Leu Glu Lys
 1040 1045 1050

Protein Complexes associated with APP-processing

Val	Glu	Gln	Glu	Thr	Trp	Arg	Glu	Thr	Gly	Ile	Ser	Phe	Val	Thr
	1055					1060					1065			
Ser	Val	Thr	Arg	Leu	Met	Glu	Arg	Leu	Leu	Asp	Tyr	Arg	Asp	Cys
	1070					1075					1080			
Met	Lys	Gly	Glu	Glu	Thr	Glu	Asn	Lys	Lys	Ile	Gly	Cys	Thr	Val
	1085					1090					1095			
Asn	Leu	Met	Asn	Phe	Tyr	Lys	Ser	Glu	Ile	Asn	Lys	Glu	Glu	Met
	1100					1105					1110			
Tyr	Ile	Arg	Tyr	Ile	His	Lys	Leu	Cys	Asp	Met	His	Leu	Gln	Ala
	1115					1120					1125			
Glu	Asn	Tyr	Thr	Glu	Ala	Ala	Phe	Thr	Leu	Leu	Leu	Tyr	Cys	Glu
	1130					1135					1140			
Leu	Leu	Gln	Trp	Glu	Asp	Arg	Pro	Leu	Arg	Glu	Phe	Leu	His	Tyr
	1145					1150					1155			
Pro	Ser	Gln	Thr	Glu	Trp	Gln	Arg	Lys	Glu	Gly	Leu	Cys	Arg	Lys
	1160					1165					1170			
Ile	Ile	His	Tyr	Phe	Asn	Lys	Gly	Lys	Ser	Trp	Glu	Phe	Gly	Ile
	1175					1180					1185			
Pro	Leu	Cys	Arg	Glu	Leu	Ala	Cys	Gln	Tyr	Glu	Ser	Leu	Tyr	Asp
	1190					1195					1200			
Tyr	Gln	Ser	Leu	Ser	Trp	Ile	Arg	Lys	Met	Glu	Ala	Ser	Tyr	Tyr
	1205					1210					1215			
Asp	Asn	Ile	Met	Glu	Gln	Gln	Arg	Leu	Glu	Pro	Glu	Phe	Phe	Arg
	1220					1225					1230			
Val	Gly	Phe	Tyr	Gly	Arg	Lys	Phe	Pro	Phe	Phe	Leu	Arg	Asn	Lys
	1235					1240					1245			
Glu	Tyr	Val	Cys	Arg	Gly	His	Asp	Tyr	Glu	Arg	Leu	Glu	Ala	Phe
	1250					1255					1260			
Gln	Gln	Arg	Met	Leu	Ser	Glu	Phe	Pro	Gln	Ala	Val	Ala	Met	Gln
	1265					1270					1275			
His	Pro	Asn	His	Pro	Asp	Asp	Ala	Ile	Leu	Gln	Cys	Asp	Ala	Gln
	1280					1285					1290			
Tyr	Leu	Gln	Ile	Tyr	Ala	Val	Thr	Pro	Ile	Pro	Asp	Tyr	Val	Asp
	1295					1300					1305			

Protein Complexes associated with APP-processing

Val Leu Gln Met Asp Arg Val Pro Asp Arg Val Lys Ser Phe Tyr
 1310 1315 1320

Arg Val Asn Asn Val Arg Lys Phe Arg Tyr Asp Arg Pro Phe His
 1325 1330 1335

Lys Gly Pro Lys Asp Lys Glu Asn Glu Phe Lys Ser Leu Trp Ile
 1340 1345 1350

Glu Arg Thr Thr Leu Thr Leu Thr His Ser Leu Pro Gly Ile Ser
 1355 1360 1365

Arg Trp Phe Glu Val Glu Arg Arg Glu Leu Val Glu Val Ser Pro
 1370 1375 1380

Leu Glu Asn Ala Ile Gln Val Val Glu Asn Lys Asn Gln Glu Leu
 1385 1390 1395

Arg Ser Leu Ile Ser Gln Tyr Gln His Lys Gln Val His Gly Asn
 1400 1405 1410

Ile Asn Leu Leu Ser Met Cys Leu Asn Gly Val Ile Asp Ala Ala
 1415 1420 1425

Val Asn Gly Gly Ile Ala Arg Tyr Gln Glu Ala Phe Phe Asp Lys
 1430 1435 1440

Asp Tyr Ile Asn Lys His Pro Gly Asp Ala Glu Lys Ile Thr Gln
 1445 1450 1455

Leu Lys Glu Leu Met Gln Glu Gln Val His Val Leu Gly Val Gly
 1460 1465 1470

Leu Ala Val His Glu Lys Phe Val His Pro Glu Met Arg Pro Leu
 1475 1480 1485

His Lys Lys Leu Ile Asp Gln Phe Gln Met Met Arg Ala Ser Leu
 1490 1495 1500

Tyr His Glu Phe Pro Gly Leu Asp Lys Leu Ser Pro Ala Cys Ser
 1505 1510 1515

Gly Thr Ser Thr Pro Arg Gly Asn Val Leu Ala Ser His Ser Pro
 1520 1525 1530

Met Ser Pro Glu Ser Ile Lys Met Thr His Arg His Ser Pro Met
 1535 1540 1545

Asn Leu Met Gly Thr Gly Arg His Ser Ser Ser Ser Leu Ser Ser
 1550 1555 1560

Protein Complexes associated with APP-processing

His Ala Ser Ser Glu Ala Gly Asn Met Val Met Leu Gly Asp Gly
 1565 1570 1575

Ser Met Gly Asp Ala Pro Glu Asp Leu Tyr His His Met Gln Leu
 1580 1585 1590

Ala Tyr Pro Asn Pro Arg Tyr Gln Gly Ser Val Thr Asn Val Ser
 1595 1600 1605

Val Leu Ser Ser Ser Gln Ala Ser Pro Ser Ser Ser Ser Leu Ser
 1610 1615 1620

Ser Thr His Ser Ala Pro Ser Gln Met Ile Thr Ser Ala Pro Ser
 1625 1630 1635

Ser Ala Arg Gly Ser Pro Ser Leu Pro Asp Lys Tyr Arg His Ala
 1640 1645 1650

Arg Glu Met Met Leu Leu Leu Pro Thr Tyr Arg Asp Arg Pro Ser
 1655 1660 1665

Ser Ala Met Tyr Pro Ala Ala Ile Leu Glu Asn Gly Gln Pro Pro
 1670 1675 1680

Asn Phe Gln Arg Ala Leu Phe Gln Gln Val Val Gly Ala Cys Lys
 1685 1690 1695

Pro Cys Ser Asp Pro Asn Leu Ser Val Ala Glu Lys Gly His Tyr
 1700 1705 1710

Ser Leu His Phe Asp Ala Phe His His Pro Leu Gly Asp Thr Pro
 1715 1720 1725

Pro Ala Leu Pro Ala Arg Thr Leu Arg Lys Ser Pro Leu His Pro
 1730 1735 1740

Ile Pro Ala Ser Pro Thr Ser Pro Gln Ser Gly Leu Asp Gly Ser
 1745 1750 1755

Asn Ser Thr Leu Ser Gly Ser Ala Ser Ser Gly Val Ser Ser Leu
 1760 1765 1770

Ser Glu Ser Asn Phe Gly His Ser Ser Glu Ala Pro Pro Arg Thr
 1775 1780 1785

Asp Thr Met Asp Ser Met Pro Ser Gln Ala Trp Asn Ala Asp Glu
 1790 1795 1800

Asp Leu Glu Pro Pro Tyr Leu Pro Val His Tyr Ser Leu Ser Glu
 1805 1810 1815

Protein Complexes associated with APP-processing

Ser Ala Val Leu Asp Ser Ile Lys Ala Gln Pro Cys Arg Ser His
 1820 1825 1830

Ser Ala Pro Gly Cys Val Ile Pro Gln Asp Pro Met Asp Pro Pro
 1835 1840 1845

Ala Leu Pro Pro Lys Pro Tyr His Pro Arg Leu Pro Ala Leu Glu
 1850 1855 1860

His Asp Glu Gly Val Leu Leu Arg Glu Glu Thr Glu Arg Pro Arg
 1865 1870 1875

Gly Leu His Arg Lys Ala Pro Leu Pro Pro Gly Ser Ala Lys Glu
 1880 1885 1890

Glu Gln Ala Arg Met Ala Trp Glu His Gly Arg Gly Glu Gln
 1895 1900 1905

<210> 112

<211> 288

<212> PRT

<213> Homo sapiens

<400> 112

Met Ala Ala Thr Phe Phe Gly Glu Val Val Lys Ala Pro Cys Arg Ala
 1 5 10 15

Gly Thr Glu Asp Glu Glu Glu Glu Glu Glu Gly Arg Arg Glu Thr Pro
 20 25 30

Glu Asp Arg Glu Val Arg Leu Gln Leu Ala Arg Lys Arg Glu Val Arg
 35 40 45

Leu Leu Arg Arg Gln Thr Lys Thr Ser Leu Glu Val Ser Leu Leu Glu
 50 55 60

Lys Tyr Pro Cys Ser Lys Phe Ile Ile Ala Ile Gly Asn Asn Ala Val
 65 70 75 80

Ala Phe Leu Ser Ser Phe Val Met Asn Ser Gly Val Trp Glu Glu Val
 85 90 95

Gly Cys Ala Lys Leu Trp Asn Glu Trp Cys Arg Thr Thr Asp Thr Thr
 100 105 110

His Leu Ser Ser Thr Glu Ala Phe Cys Val Phe Tyr His Leu Lys Ser
 115 120 125

Protein Complexes associated with APP-processing
 Asn Pro Ser Val Phe Leu Cys Gln Cys Ser Cys Tyr Val Ala Glu Asp
 130 135 140

Gln Gln Tyr Gln Trp Leu Glu Lys Val Phe Gly Ser Cys Pro Arg Lys
 145 150 155 160

Asn Met Gln Ile Thr Ile Leu Thr Cys Arg His Val Thr Asp Tyr Lys
 165 170 175

Thr Ser Glu Ser Thr Gly Ser Leu Pro Ser Pro Phe Leu Arg Ala Leu
 180 185 190

Lys Thr Gln Asn Phe Lys Asp Ser Ala Cys Cys Pro Leu Leu Glu Gln
 195 200 205

Pro Asn Ile Val His Asp Leu Pro Ala Ala Val Leu Ser Tyr Cys Gln
 210 215 220

Val Trp Lys Ile Pro Ala Ile Leu Tyr Leu Cys Tyr Thr Asp Val Met
 225 230 235 240

Lys Leu Asp Leu Ile Thr Val Glu Ala Phe Lys Pro Ile Leu Ser Thr
 245 250 255

Arg Ser Leu Lys Gly Leu Val Lys Asn Ile Pro Gln Ser Thr Glu Ile
 260 265 270

Leu Lys Lys Leu Met Thr Thr Asn Glu Ile Gln Ser Asn Ile Tyr Thr
 275 280 285

<210> 113

<211> 431

<212> PRT

<213> Homo sapiens

<400> 113

Met Ser Trp Val Gln Ala Thr Leu Leu Ala Arg Gly Leu Cys Arg Ala
 1 5 10 15

Trp Gly Gly Thr Cys Gly Ala Ala Leu Thr Gly Thr Ser Ile Ser Gln
 20 25 30

Val Pro Arg Arg Leu Pro Arg Gly Leu His Cys Ser Ala Ala Ala His
 35 40 45

Ser Ser Glu Gln Ser Leu Val Pro Ser Pro Pro Glu Pro Arg Gln Arg
 50 55 60

Protein Complexes associated with APP-processing

Pro Thr Lys Ala Leu Val Pro Phe Glu Asp Leu Phe Gly Gln Ala Pro
 65 70 75 80

Gly Gly Glu Arg Asp Lys Ala Ser Phe Leu Gln Thr Val Gln Lys Phe
 85 90 95

Ala Glu His Ser Val Arg Lys Arg Gly His Ile Asp Phe Ile Tyr Leu
 100 105 110

Ala Leu Arg Lys Met Arg Glu Tyr Gly Val Glu Arg Asp Leu Ala Val
 115 120 125

Tyr Asn Gln Leu Leu Asn Ile Phe Pro Lys Glu Val Phe Arg Pro Arg
 130 135 140

Asn Ile Ile Gln Arg Ile Phe Val His Tyr Pro Arg Gln Gln Glu Cys
 145 150 155 160

Gly Ile Ala Val Leu Glu Gln Met Glu Asn His Gly Val Met Pro Asn
 165 170 175

Lys Glu Thr Glu Phe Leu Leu Ile Gln Ile Phe Gly Arg Lys Ser Tyr
 180 185 190

Pro Met Leu Lys Leu Val Arg Leu Lys Leu Trp Phe Pro Arg Phe Met
 195 200 205

Asn Val Asn Pro Phe Pro Val Pro Arg Asp Leu Pro Gln Asp Pro Val
 210 215 220

Glu Leu Ala Met Phe Gly Leu Arg His Met Glu Pro Asp Leu Ser Ala
 225 230 235 240

Arg Val Thr Ile Tyr Gln Val Pro Leu Pro Lys Asp Ser Thr Gly Ala
 245 250 255

Ala Asp Pro Pro Gln Pro His Ile Val Gly Ile Gln Ser Pro Asp Gln
 260 265 270

Gln Ala Ala Leu Ala Arg His Asn Pro Ala Arg Pro Val Phe Val Glu
 275 280 285

Gly Pro Phe Ser Leu Trp Leu Arg Asn Lys Cys Val Tyr Tyr His Ile
 290 295 300

Leu Arg Ala Asp Leu Leu Pro Pro Glu Glu Arg Glu Val Glu Glu Thr
 305 310 315 320

Pro Glu Glu Trp Asn Leu Tyr Tyr Pro Met Gln Leu Asp Leu Glu Tyr
 325 330 335

Protein Complexes associated with APP-processing
 Val Arg Ser Gly Trp Asp Asn Tyr Glu Phe Asp Ile Asn Glu Val Glu
 340 345 350

Glu Gly Pro Val Phe Ala Met Cys Met Ala Gly Ala His Asp Gln Ala
 355 360 365

Thr Met Ala Lys Trp Ile Gln Gly Leu Gln Glu Thr Asn Pro Thr Leu
 370 375 380

Ala Gln Ile Pro Val Val Phe Arg Leu Ala Gly Ser Thr Arg Glu Leu
 385 390 395 400

Gln Thr Ser Ser Ala Gly Leu Glu Glu Pro Pro Leu Pro Glu Asp His
 405 410 415

Gln Glu Glu Asp Asp Asn Leu Gln Arg Gln Gln Gln Gly Gln Ser
 420 425 430

<210> 114

<211> 579

<212> PRT

<213> Homo sapiens

<400> 114

Met Pro Ser Ala Ser Cys Asp Thr Leu Leu Asp Asp Ile Glu Asp Ile
 1 5 10 15

Val Ser Gln Glu Asp Ser Lys Pro Gln Asp Arg His Phe Val Arg Lys
 20 25 30

Asp Val Val Pro Lys Val Arg Arg Arg Asn Thr Gln Lys Tyr Leu Gln
 35 40 45

Glu Glu Glu Asn Ser Pro Pro Ser Asp Ser Thr Ile Pro Gly Ile Gln
 50 55 60

Lys Ile Trp Ile Arg Thr Trp Gly Cys Ser His Asn Asn Ser Asp Gly
 65 70 75 80

Glu Tyr Met Ala Gly Gln Leu Ala Ala Tyr Gly Tyr Lys Ile Thr Glu
 85 90 95

Asn Ala Ser Asp Ala Asp Leu Trp Leu Leu Asn Ser Cys Thr Val Lys
 100 105 110

Asn Pro Ala Glu Asp His Phe Arg Asn Ser Ile Lys Lys Ala Gln Glu
 115 120 125

Protein Complexes associated with APP-processing

Glu Asn Lys Lys Ile Val Leu Ala Gly Cys Val Pro Gln Ala Gln Pro
 130 135 140

Arg Gln Asp Tyr Leu Lys Gly Leu Ser Ile Ile Gly Val Gln Gln Ile
 145 150 155 160

Asp Arg Val Val Glu Val Val Glu Glu Thr Ile Lys Gly His Ser Val
 165 170 175

Arg Leu Leu Gly Gln Lys Lys Asp Asn Gly Arg Arg Leu Gly Gly Ala
 180 185 190

Arg Leu Asp Leu Pro Lys Ile Arg Lys Asn Pro Leu Ile Glu Ile Ile
 195 200 205

Ser Ile Ser Thr Gly Cys Leu Asn Ala Cys Thr Tyr Cys Lys Thr Lys
 210 215 220

His Ala Arg Gly Asn Leu Ala Ser Tyr Pro Ile Asp Glu Leu Val Asp
 225 230 235 240

Arg Ala Lys Gln Ser Phe Gln Glu Gly Val Cys Glu Ile Trp Leu Thr
 245 250 255

Ser Glu Asp Thr Gly Ala Tyr Gly Arg Asp Ile Gly Thr Asn Leu Pro
 260 265 270

Thr Leu Leu Trp Lys Leu Val Glu Val Ile Pro Glu Gly Ala Met Leu
 275 280 285

Arg Leu Gly Met Thr Asn Pro Pro Tyr Ile Leu Glu His Leu Glu Glu
 290 295 300

Met Ala Lys Ile Leu Asn His Pro Arg Val Tyr Ala Phe Leu His Ile
 305 310 315 320

Pro Val Gln Ser Ala Ser Asp Ser Val Leu Met Glu Met Lys Arg Glu
 325 330 335

Tyr Cys Val Ala Asp Phe Lys Arg Val Val Asp Phe Leu Lys Glu Lys
 340 345 350

Val Pro Gly Ile Thr Ile Ala Thr Asp Ile Ile Cys Gly Phe Pro Gly
 355 360 365

Glu Thr Asp Gln Asp Phe Gln Glu Thr Val Lys Leu Val Glu Glu Tyr
 370 375 380

Lys Phe Pro Ser Leu Phe Ile Asn Gln Phe Tyr Pro Arg Pro Gly Thr
 385 390 395 400

Protein Complexes associated with APP-processing

Pro	Ala	Ala	Lys	Met	Glu	Gln	Val	Pro	Ala	Gln	Val	Lys	Lys	Gln	Arg
				405				410						415	

Val Tyr Asn

<213> Homo sapiens

<400> 115

Asn Glu Asn Ile Thr Val Val Lys Gly Ile Arg Leu Ser Glu Asn Val
20 25 30

Protein Complexes associated with APP-processing

Ile Asp Arg Met Lys Glu Ser Ser Pro Ser Gly Ser Lys Ser Gln Arg
 35 40 45

Tyr Ser Gly Ala Tyr Gly Ala Ser Val Ser Asp Glu Glu Leu Lys Arg
 50 55 60

Arg Val Ala Glu Glu Leu Ala Leu Glu Gln Ala Lys Lys Glu Ser Glu
 65 70 75 80

Asp Gln Lys Arg Leu Lys Gln Ala Lys Glu Leu Asp Arg Glu Arg Ala
 85 90 95

Ala Ala Asn Glu Gln Leu Thr Arg Ala Ile Leu Arg Glu Arg Ile Cys
 100 105 110

Ser Glu Glu Glu Arg Ala Lys Ala Lys His Leu Ala Arg Gln Leu Glu
 115 120 125

Glu Lys Asp Arg Val Leu Lys Lys Gln Asp Ala Phe Tyr Lys Glu Gln
 130 135 140

Leu Ala Arg Leu Glu Glu Arg Ser Ser Glu Phe Tyr Arg Val Thr Thr
 145 150 155 160

Glu Gln Tyr Gln Lys Ala Ala Glu Glu Val Glu Ala Lys Phe Lys Arg
 165 170 175

Tyr Glu Ser His Pro Val Cys Ala Asp Leu Gln Ala Lys Ile Leu Gln
 180 185 190

Cys Tyr Arg Glu Asn Thr His Gln Thr Leu Lys Cys Ser Ala Leu Ala
 195 200 205

Thr Gln Tyr Met His Cys Val Asn His Ala Lys Gln Ser Met Leu Glu
 210 215 220

Lys Gly Gly
 225

<210> 116

<211> 291

<212> PRT

<213> Homo sapiens

<400> 116

Met Ala Leu Ala Ala Arg Leu Leu Pro Gln Phe Leu His Ser Arg Ser
 1 5 10 15

Protein Complexes associated with APP-processing

Leu Pro Cys Gly Ala Val Arg Leu Arg Thr Pro Ala Val Ala Glu Val
 20 25 30

Arg Leu Pro Ser Ala Thr Leu Cys Tyr Phe Cys Arg Cys Arg Leu Gly
 35 40 45

Leu Gly Ala Ala Leu Phe Pro Arg Ser Ala Arg Ala Leu Ala Ala Ser
 50 55 60

Ala Leu Pro Ala Gln Gly Ser Arg Trp Pro Val Leu Ser Ser Pro Gly
 65 70 75 80

Leu Pro Ala Ala Phe Ala Ser Phe Pro Ala Cys Pro Gln Arg Ser Tyr
 85 90 95

Ser Thr Glu Glu Lys Pro Gln Gln His Gln Lys Thr Lys Met Ile Val
 100 105 110

Leu Gly Phe Ser Asn Pro Ile Asn Trp Val Arg Thr Arg Ile Lys Ala
 115 120 125

Phe Leu Ile Trp Ala Tyr Phe Asp Lys Glu Phe Ser Ile Thr Glu Phe
 130 135 140

Ser Glu Gly Ala Lys Gln Ala Phe Ala His Val Ser Lys Leu Leu Ser
 145 150 155 160

Gln Cys Lys Phe Asp Leu Leu Glu Glu Leu Val Ala Lys Glu Val Leu
 165 170 175

His Ala Leu Lys Glu Lys Val Thr Ser Leu Pro Asp Asn His Lys Asn
 180 185 190

Ala Leu Ala Ala Asn Ile Asp Glu Ile Val Phe Thr Ser Thr Gly Asp
 195 200 205

Ile Ser Ile Tyr Tyr Asp Glu Lys Gly Arg Lys Phe Val Asn Ile Leu
 210 215 220

Met Cys Phe Trp Tyr Leu Thr Ser Ala Asn Ile Pro Ser Glu Thr Leu
 225 230 235 240

Arg Gly Ala Ser Val Phe Gln Val Lys Leu Gly Asn Gln Asn Val Glu
 245 250 255

Thr Lys Gln Leu Leu Ser Ala Ser Tyr Glu Phe Gln Arg Glu Phe Thr
 260 265 270

Gln Gly Val Lys Pro Asp Trp Thr Ile Ala Arg Ile Glu His Ser Lys
 275 280 285

Protein Complexes associated with APP-processing

Leu Leu Glu
290

<210> 117

<211> 522

<212> PRT

<213> Homo sapiens

<400> 117

Met Leu Leu Gln Gln Leu Arg Pro His Leu Glu Gly Cys Arg Asn Asp
1 5 10 15

Ile Val Ser Ala Arg Pro Asp Glu Trp Leu Gly Arg Cys Ile Leu Asp
20 25 30

Ala Thr Gly Val Gly Cys Thr Gly Asp His Glu Gly Val His Tyr Ser
35 40 45

His Leu Glu Leu Ser Pro Gly Glu Pro Val Gln Glu Gly Asp Pro His
50 55 60

Phe Arg Ser Ala Leu Thr Ala His Pro Val Arg Asp Pro Val His Met
65 70 75 80

Tyr Gln Leu His Lys Ala Phe Ala Arg Ala Glu Leu Glu Arg Thr Tyr
85 90 95

Gln Glu Ile Gln Glu Leu Gln Trp Glu Ile Gln Asn Thr Ser His Leu
100 105 110

Ala Val Asp Gly Asp Arg Ala Ala Ala Trp Pro Val Gly Ile Pro Ala
115 120 125

Pro Ser Arg Pro Ala Ser Arg Phe Glu Val Leu Arg Trp Asp Tyr Phe
130 135 140

Thr Glu Gln His Ala Phe Ser Cys Ala Asp Gly Ser Pro Arg Cys Pro
145 150 155 160

Leu Arg Gly Ala Asp Arg Ala Asp Val Ala Asp Val Leu Gly Thr Ala
165 170 175

Leu Glu Glu Leu Asn Arg Arg Tyr His Pro Ala Leu Arg Leu Gln Lys
180 185 190

Gln Gln Leu Val Asn Gly Tyr Arg Arg Phe Asp Pro Ala Arg Gly Met
195 200 205

Protein Complexes associated with APP-processing
 Glu Tyr Thr Leu Asp Leu Gln Leu Glu Ala Leu Thr Pro Gln Gly Gly
 210 215 220

Arg Arg Pro Leu Thr Arg Arg Val Gln Leu Leu Arg Pro Leu Ser Arg
 225 230 235 240

Val Glu Ile Leu Pro Val Pro Tyr Val Thr Glu Ala Ser Arg Leu Thr
 245 250 255

Val Leu Leu Pro Leu Ala Ala Ala Glu Arg Asp Leu Ala Pro Gly Phe
 260 265 270

Leu Glu Ala Phe Ala Thr Ala Ala Leu Glu Pro Gly Asp Ala Ala Ala
 275 280 285

Ala Leu Thr Leu Leu Leu Leu Tyr Glu Pro Arg Gln Ala Gln Arg Val
 290 295 300

Ala His Ala Asp Val Phe Ala Pro Val Lys Ala His Val Ala Glu Leu
 305 310 315 320

Glu Arg Arg Phe Pro Gly Ala Arg Val Pro Trp Leu Ser Val Gln Thr
 325 330 335

Ala Ala Pro Ser Pro Leu Arg Leu Met Asp Leu Leu Ser Lys Lys His
 340 345 350

Pro Leu Asp Thr Leu Phe Leu Leu Ala Gly Pro Asp Thr Val Leu Thr
 355 360 365

Pro Asp Phe Leu Asn Arg Cys Arg Met His Ala Ile Ser Gly Trp Gln
 370 375 380

Ala Phe Phe Pro Met His Phe Gln Ala Phe His Pro Ala Val Ala Pro
 385 390 395 400

Pro Gln Gly Pro Gly Pro Pro Glu Leu Gly Arg Asp Thr Gly Arg Phe
 405 410 415

Asp Arg Gln Ala Ala Ser Glu Ala Cys Phe Tyr Asn Ser Asp Tyr Val
 420 425 430

Ala Ala Arg Gly Arg Leu Ala Ala Ala Ser Glu Gln Glu Glu Glu Leu
 435 440 445

Leu Glu Ser Leu Asp Val Tyr Glu Leu Phe Leu His Phe Ser Ser Leu
 450 455 460

His Val Leu Arg Ala Val Glu Pro Ala Leu Leu Gln Arg Tyr Arg Ala
 465 470 475 480

Protein Complexes associated with APP-processing

Gln Thr Cys Ser Ala Arg Leu Ser Glu Asp Leu Tyr His Arg Cys Leu
 485 490 495

Gln Ser Val Leu Glu Gly Leu Gly Ser Arg Thr Gln Leu Ala Met Leu
 500 505 510

Leu Phe Glu Gln Glu Gln Gly Asn Ser Thr
 515 520

<210> 118

<211> 335

<212> PRT

<213> Homo sapiens

<400> 118

Met Lys Leu Lys Leu Lys Asn Val Phe Leu Ala Tyr Phe Leu Val Ser
 1 5 10 15

Ile Ala Gly Leu Leu Tyr Ala Leu Val Gln Leu Gly Gln Pro Cys Asp
 20 25 30

Cys Leu Pro Pro Leu Arg Ala Ala Ala Glu Gln Leu Arg Gln Lys Asp
 35 40 45

Leu Arg Ile Ser Gln Leu Gln Ala Glu Leu Arg Arg Pro Pro Pro Ala
 50 55 60

Pro Ala Gln Pro Pro Glu Pro Glu Ala Leu Pro Thr Ile Tyr Val Val
 65 70 75 80

Thr Pro Thr Tyr Ala Arg Leu Val Gln Lys Ala Glu Leu Val Arg Leu
 85 90 95

Ser Gln Thr Leu Ser Leu Val Pro Arg Leu His Trp Leu Leu Val Glu
 100 105 110

Asp Ala Glu Gly Pro Thr Pro Leu Val Ser Gly Leu Leu Ala Ala Ser
 115 120 125

Gly Leu Leu Phe Thr His Leu Val Val Leu Thr Pro Lys Ala Gln Arg
 130 135 140

Leu Arg Glu Gly Glu Pro Gly Trp Val His Pro Arg Gly Val Glu Gln
 145 150 155 160

Arg Asn Lys Ala Leu Asp Trp Leu Arg Gly Arg Gly Gly Ala Val Gly
 165 170 175

Protein Complexes associated with APP-processing

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Protein Complexes associated with APP-processing

Val Thr Glu Pro Arg Ala Cys Leu Thr Ser Gly Thr Pro Gly Pro Arg
 65 70 75 80

Ala Gln Leu Thr Ala Val Thr Pro Asp Thr Arg Thr Arg Glu Ala Ser
 85 90 95

Glu Asn Ser Gly Thr Arg Ser Arg Ala Trp Leu Ala Val Ala Leu Gly
 100 105 110

Ala Gly Gly Ala Val Leu Leu Leu Leu Trp Gly Gly Gly Arg Gly Pro
 115 120 125

Pro Ala Val Leu Ala Ala Val Pro Ser Pro Pro Pro Ala Ser Pro Arg
 130 135 140

Ser Gln Tyr Asn Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala
 145 150 155 160

Val Val Tyr Ile Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu
 165 170 175

Val Pro Ile Ser Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu
 180 185 190

Ile Val Thr Asn Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val
 195 200 205

Arg Leu Leu Ser Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp
 210 215 220

Pro Val Ala Asp Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu
 225 230 235 240

Pro Thr Leu Pro Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe
 245 250 255

Val Val Ala Met Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser
 260 265 270

Gly Ile Val Ser Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro
 275 280 285

Gln Thr Asn Val Glu Tyr Ile Gln Thr Asp Ala Ala Ile Asp Phe Gly
 290 295 300

Asn Ser Gly Gly Pro Leu Val Asn Leu Asp Gly Glu Val Ile Gly Val
 305 310 315 320

Asn Thr Met Lys Val Thr Ala Gly Ile Ser Phe Ala Ile Pro Ser Asp
 325 330 335

Protein Complexes associated with APP-processing

protein Complexes associated with APP-processing

Gly Ile Ser Gly Ser Gln Arg Arg Tyr Ile Gly Val Met Met Leu Thr
355 360 365

Leu Ser Pro Ser Ile Leu Ala Glu Leu Gln Leu Arg Glu Pro Ser Phe
370 375 380

Pro 385 Asp Val Gln His Gly 390 Val Leu Ile His Lys 395 Val Ile Leu Gly Ser 400

Pro Ala His Arg Ala Gly Leu Arg Pro Gly Asp Val Ile Leu Ala Ile
405 410 415

Gly Glu Gln Met Val Gln Asn Ala Glu Asp Val Tyr Glu Ala Val Arg
420 425 430

Thr Gln Ser Gln Leu Ala Val Gln Ile Arg Arg Gly Arg Glu Thr Leu
435 440 445

Thr Leu Tyr Val Thr Pro Glu Val Thr Glu
450 455

$\langle 210 \rangle$ 120

<211> 437

<212> PRT

<213> Homo sapiens

<400> 120

Met Thr Gln Leu Phe Leu Trp Glu Tyr Gly Asp Leu His Leu Phe Gly
1 5 10 15

Pro Asn Gln Arg Pro Ala Pro Cys Tyr Asp Pro Cys Glu Ala Val Leu
20 25 30

Val Glu Ser Ile Pro Glu Gly Leu Asp Phe Pro Asn Ala Ser Thr Gly
35 40 45

Asn Pro Ser Thr Ser Gln Ala Trp Leu Gly Leu Leu Ala Gly Ala His
50 55 60

Ser Ser Leu Asp Ile Ala Ser Phe Tyr Trp Thr Leu Thr Asn Asn Asp
65 70 75 80

Thr His Thr Gln Glu Pro Ser Ala Gln Gln Gly Glu Glu Val Leu Arg
85 90 95

Protein Complexes associated with APP-processing

Gln Leu Gln Thr Leu Ala Pro Lys Gly Val Asn Val Arg Ile Ala Val
 100 105 110

Ser Lys Pro Ser Gly Pro Gln Pro Gln Ala Asp Leu Gln Ala Leu Leu
 115 120 125

Gln Ser Gly Ala Gln Val Arg Met Val Asp Met Gln Lys Leu Thr His
 130 135 140

Gly Val Leu His Thr Lys Phe Trp Val Val Asp Gln Thr His Phe Tyr
 145 150 155 160

Leu Gly Ser Ala Asn Met Asp Trp Arg Ser Leu Thr Gln Val Lys Glu
 165 170 175

Leu Gly Val Val Met Tyr Asn Cys Ser Cys Leu Ala Arg Asp Leu Thr
 180 185 190

Lys Ile Phe Glu Ala Tyr Trp Phe Leu Gly Gln Ala Gly Ser Ser Ile
 195 200 205

Pro Ser Thr Trp Pro Arg Phe Tyr Asp Thr Arg Tyr Asn Gln Glu Thr
 210 215 220

Pro Met Glu Ile Cys Leu Asn Gly Thr Pro Ala Leu Ala Tyr Leu Ala
 225 230 235 240

Ser Ala Pro Pro Pro Leu Cys Pro Ser Gly Arg Thr Pro Asp Leu Lys
 245 250 255

Ala Leu Leu Asn Val Val Asp Asn Ala Arg Ser Phe Ile Tyr Val Ala
 260 265 270

Val Met Asn Tyr Leu Pro Thr Leu Glu Phe Ser His Pro His Arg Phe
 275 280 285

Trp Pro Ala Ile Asp Asp Gly Leu Arg Arg Ala Thr Tyr Glu Arg Gly
 290 295 300

Val Lys Val Arg Leu Leu Ile Ser Cys Trp Gly His Ser Glu Pro Ser
 305 310 315 320

Met Arg Ala Phe Leu Leu Ser Leu Ala Ala Leu Arg Asp Asn His Thr
 325 330 335

His Ser Asp Ile Gln Val Lys Leu Phe Val Val Pro Ala Asp Glu Ala
 340 345 350

Gln Ala Arg Ile Pro Tyr Ala Arg Val Asn His Asn Lys Tyr Met Val
 355 360 365

Protein Complexes associated with APP-processing
 Thr Glu Arg Ala Thr Tyr Ile Gly Thr Ser Asn Trp Ser Gly Asn Tyr
 370 375 380

Phe Thr Glu Thr Ala Gly Thr Ser Leu Leu Val Thr Gln Asn Gly Arg
 385 390 395 400

Gly Gly Leu Arg Ser Gln Leu Glu Ala Ile Phe Leu Arg Asp Trp Asp
 405 410 415

Ser Pro Tyr Ile His Asp Leu Asp Thr Ser Ala Asp Ser Val Gly Asn
 420 425 430

Ala Cys Arg Leu Leu
 435

<210> 121

<211> 531

<212> PRT

<213> Homo sapiens

<400> 121

Arg Val Tyr Ala Asp Ala Pro Ala Lys Leu Leu Leu Pro Pro Pro Ala
 1 5 10 15

Ala Trp Asp Leu Ala Val Arg Leu Arg Gly Ala Glu Ala Ala Ser Glu
 20 25 30

Arg Gln Val Tyr Ser Val Thr Met Lys Leu Leu Leu Leu His Pro Ala
 35 40 45

Phe Gln Ser Cys Leu Leu Leu Thr Leu Leu Gly Leu Trp Arg Thr Thr
 50 55 60

Pro Glu Ala His Ala Ser Ser Leu Gly Ala Pro Ala Ile Ser Ala Ala
 65 70 75 80

Ser Phe Leu Gln Asp Leu Ile His Arg Tyr Gly Glu Gly Asp Ser Leu
 85 90 95

Thr Leu Gln Gln Leu Lys Ala Leu Leu Asn His Leu Asp Val Gly Val
 100 105 110

Gly Arg Gly Asn Val Thr Gln His Val Gln Gly His Arg Asn Leu Ser
 115 120 125

Thr Cys Phe Ser Ser Gly Asp Leu Phe Thr Ala His Asn Phe Ser Glu
 130 135 140

Protein Complexes associated with APP-processing

Gln Ser Arg Ile Gly Ser Ser Glu Leu Gln Glu Phe Cys Pro Thr Ile
 145 150 155 160

Leu Gln Gln Leu Asp Ser Arg Ala Cys Thr Ser Glu Asn Gln Glu Asn
 165 170 175

Glu Glu Asn Glu Gln Thr Glu Glu Gly Arg Pro Ser Ala Val Glu Val
 180 185 190

Trp Gly Tyr Gly Leu Leu Cys Val Thr Val Ile Ser Leu Cys Ser Leu
 195 200 205

Leu Gly Ala Ser Val Val Pro Phe Met Lys Lys Thr Phe Tyr Lys Arg
 210 215 220

Leu Leu Leu Tyr Phe Ile Ala Leu Ala Ile Gly Thr Leu Tyr Ser Asn
 225 230 235 240

Ala Leu Phe Gln Leu Ile Pro Glu Ala Phe Gly Phe Asn Pro Leu Glu
 245 250 255

Asp Tyr Tyr Val Ser Lys Ser Ala Val Val Phe Gly Gly Phe Tyr Leu
 260 265 270

Phe Phe Phe Thr Glu Lys Ile Leu Lys Ile Leu Leu Lys Gln Lys Asn
 275 280 285

Glu His His His Gly His Ser His Tyr Ala Ser Glu Ser Leu Pro Ser
 290 295 300

Lys Lys Asp Gln Glu Glu Gly Val Met Glu Lys Leu Gln Asn Gly Asp
 305 310 315 320

Leu Asp His Met Ile Pro Gln His Cys Ser Ser Glu Leu Asp Gly Lys
 325 330 335

Ala Pro Met Val Asp Glu Lys Val Ile Val Gly Ser Leu Ser Val Gln
 340 345 350

Asp Leu Gln Ala Ser Gln Ser Ala Cys Tyr Trp Leu Lys Gly Val Arg
 355 360 365

Tyr Ser Asp Ile Gly Thr Leu Ala Trp Met Ile Thr Leu Ser Asp Gly
 370 375 380

Leu His Asn Phe Ile Asp Gly Leu Ala Ile Gly Ala Ser Phe Thr Val
 385 390 395 400

Ser Val Phe Gln Gly Ile Ser Thr Ser Val Ala Ile Leu Cys Glu Glu
 405 410 415

Protein Complexes associated with APP-processing

Phe Pro His Glu Leu Gly Asp Phe Val Ile Leu Leu Asn Ala Gly Met
 420 425 430

Ser Ile Gln Gln Ala Leu Phe Phe Asn Phe Leu Ser Ala Cys Cys Cys
 435 440 445

Tyr Leu Gly Leu Ala Phe Gly Ile Leu Ala Gly Ser His Phe Ser Ala
 450 455 460

Asn Trp Ile Phe Ala Leu Ala Gly Gly Met Phe Leu Tyr Ile Ser Leu
 465 470 475 480

Ala Asp Met Phe Pro Glu Met Asn Glu Val Cys Gln Glu Asp Glu Arg
 485 490 495

Lys Gly Ser Ile Leu Ile Pro Phe Ile Ile Gln Asn Leu Gly Leu Leu
 500 505 510

Thr Gly Phe Thr Ile Met Val Val Leu Thr Met Tyr Ser Gly Gln Ile
 515 520 525

Gln Ile Gly
 530

<210> 122
 <211> 993
 <212> PRT
 <213> Homo sapiens

<400> 122

Met Ala Ala Glu Trp Ala Ser Arg Phe Trp Leu Trp Ala Thr Leu Leu
 1 5 10 15

Ile Pro Ala Ala Ala Val Tyr Glu Asp Gln Val Gly Lys Phe Asp Trp
 20 25 30

Arg Gln Gln Tyr Val Gly Lys Val Lys Phe Ala Ser Leu Glu Phe Ser
 35 40 45

Pro Gly Ser Lys Lys Leu Val Val Ala Thr Glu Lys Asn Val Ile Ala
 50 55 60

Ala Leu Asn Ser Arg Thr Gly Glu Ile Leu Trp Arg His Val Asp Lys
 65 70 75 80

Gly Thr Ala Glu Gly Ala Val Asp Ala Met Leu Leu His Gly Gln Asp
 85 90 95

Protein Complexes associated with APP-processing
 Val Ile Thr Val Ser Asn Gly Gly Arg Ile Met Arg Ser Trp Glu Thr
 100 105 110

Asn Ile Gly Gly Leu Asn Trp Glu Ile Thr Leu Asp Ser Gly Ser Phe
 115 120 125

Gln Ala Leu Gly Leu Val Gly Leu Gln Glu Ser Val Arg Tyr Ile Ala
 130 135 140

Val Leu Lys Lys Thr Thr Leu Ala Leu His His Leu Ser Ser Gly His
 145 150 155 160

Leu Lys Trp Val Glu His Leu Pro Glu Ser Asp Ser Ile His Tyr Gln
 165 170 175

Met Val Tyr Ser Tyr Gly Ser Gly Val Val Trp Ala Leu Gly Val Val
 180 185 190

Pro Phe Ser His Val Asn Ile Val Lys Phe Asn Val Glu Asp Gly Glu
 195 200 205

Ile Val Gln Gln Val Arg Val Ser Thr Pro Trp Leu Gln His Leu Ser
 210 215 220

Gly Ala Cys Gly Val Val Asp Glu Ala Val Leu Val Cys Pro Asp Pro
 225 230 235 240

Ser Ser Arg Ser Leu Gln Thr Leu Ala Leu Glu Thr Glu Trp Glu Leu
 245 250 255

Arg Gln Ile Pro Leu Gln Ser Leu Asp Leu Glu Phe Gly Ser Gly Phe
 260 265 270

Gln Pro Arg Val Leu Pro Thr Gln Pro Asn Pro Val Asp Ala Ser Arg
 275 280 285

Ala Gln Phe Phe Leu His Leu Ser Pro Ser His Tyr Ala Leu Leu Gln
 290 295 300

Tyr His Tyr Gly Thr Leu Ser Leu Leu Lys Asn Phe Pro Gln Thr Ala
 305 310 315 320

Leu Val Ser Phe Ala Thr Thr Gly Glu Lys Thr Val Ala Ala Val Met
 325 330 335

Ala Cys Arg Asn Glu Val Gln Lys Ser Ser Ser Ser Glu Asp Gly Ser
 340 345 350

Met Gly Ser Phe Ser Glu Lys Ser Ser Ser Lys Asp Ser Leu Ala Cys
 355 360 365

Protein Complexes associated with APP-processing
 Phe Asn Gln Thr Tyr Thr Ile Asn Leu Tyr Leu Val Glu Thr Gly Arg
 370 375 380

Arg Leu Leu Asp Thr Thr Ile Thr Phe Ser Leu Glu Gln Ser Gly Thr
 385 390 395 400

Arg Pro Glu Arg Leu Tyr Ile Gln Val Phe Leu Lys Lys Asp Asp Ser
 405 410 415

Val Gly Tyr Arg Ala Leu Val Gln Thr Glu Asp His Leu Leu Leu Phe
 420 425 430

Leu Gln Gln Leu Ala Gly Lys Val Val Leu Trp Ser Arg Glu Glu Ser
 435 440 445

Leu Ala Glu Val Val Cys Leu Glu Met Val Asp Leu Pro Leu Thr Gly
 450 455 460

Ala Gln Ala Glu Leu Glu Gly Glu Phe Gly Lys Lys Ala Asp Gly Leu
 465 470 475 480

Leu Gly Met Phe Leu Lys Arg Leu Ser Ser Gln Leu Ile Leu Leu Gln
 485 490 495

Ala Trp Thr Ser His Leu Trp Lys Met Phe Tyr Asp Ala Arg Lys Pro
 500 505 510

Arg Ser Gln Ile Lys Asn Glu Ile Asn Ile Asp Thr Leu Ala Arg Asp
 515 520 525

Glu Phe Asn Leu Gln Lys Met Met Val Met Val Thr Ala Ser Gly Lys
 530 535 540

Leu Phe Gly Ile Glu Ser Ser Ser Gly Thr Ile Leu Trp Lys Gln Tyr
 545 550 555 560

Leu Pro Asn Val Lys Pro Asp Ser Ser Phe Lys Leu Met Val Gln Arg
 565 570 575

Thr Thr Ala His Phe Pro His Pro Pro Gln Cys Thr Leu Leu Val Lys
 580 585 590

Asp Lys Glu Ser Gly Met Ser Ser Leu Tyr Val Phe Asn Pro Ile Phe
 595 600 605

Gly Lys Trp Ser Gln Val Ala Pro Pro Val Leu Lys Arg Pro Ile Leu
 610 615 620

Gln Ser Leu Leu Leu Pro Val Met Asp Gln Asp Tyr Ala Lys Val Leu
 625 630 635 640

Protein Complexes associated with APP-processing
 Leu Leu Ile Asp Asp Glu Tyr Lys Val Thr Ala Phe Pro Ala Thr Arg
 645 650 655

Asn Val Leu Arg Gln Leu His Glu Leu Ala Pro Ser Ile Phe Phe Tyr
 660 665 670

Leu Val Asp Ala Glu Gln Gly Arg Leu Cys Gly Tyr Arg Leu Arg Lys
 675 680 685

Asp Leu Thr Thr Glu Leu Ser Trp Glu Leu Thr Ile Pro Pro Glu Val
 690 695 700

Gln Arg Ile Val Lys Val Lys Gly Lys Arg Ser Ser Glu His Val His
 705 710 715 720

Ser Gln Gly Arg Val Met Gly Asp Arg Ser Val Leu Tyr Lys Ser Leu
 725 730 735

Asn Pro Asn Leu Leu Ala Val Val Thr Glu Ser Thr Asp Ala His His
 740 745 750

Glu Arg Thr Phe Ile Gly Ile Phe Leu Ile Asp Gly Val Thr Gly Arg
 755 760 765

Ile Ile His Ser Ser Val Gln Lys Lys Ala Lys Gly Pro Val His Ile
 770 775 780

Val His Ser Glu Asn Trp Val Val Tyr Gln Tyr Trp Asn Thr Lys Ala
 785 790 795 800

Arg Arg Asn Glu Phe Thr Val Leu Glu Leu Tyr Glu Gly Thr Glu Gln
 805 810 815

Tyr Asn Ala Thr Ala Phe Ser Ser Leu Asp Arg Pro Gln Leu Pro Gln
 820 825 830

Val Leu Gln Gln Ser Tyr Ile Phe Pro Ser Ser Ile Ser Ala Met Glu
 835 840 845

Ala Thr Ile Thr Glu Arg Gly Ile Thr Ser Arg His Leu Leu Ile Gly
 850 855 860

Leu Pro Ser Gly Ala Ile Leu Ser Leu Pro Lys Ala Leu Leu Asp Pro
 865 870 875 880

Arg Arg Pro Glu Ile Pro Thr Glu Gln Ser Arg Glu Glu Asn Leu Ile
 885 890 895

Pro Tyr Ser Pro Asp Val Gln Ile His Ala Glu Arg Phe Ile Asn Tyr
 900 905 910

Protein Complexes associated with APP-processing
 Asn Gln Thr Val Ser Arg Met Arg Gly Ile Tyr Thr Ala Pro Ser Gly
 915 920 925

Leu Glu Ser Thr Cys Leu Val Val Ala Tyr Gly Leu Asp Ile Tyr Gln
 930 935 940

Thr Arg Val Tyr Pro Ser Lys Gln Phe Asp Val Leu Lys Asp Asp Tyr
 945 950 955 960

Asp Tyr Val Leu Ile Ser Ser Val Leu Phe Gly Leu Val Phe Ala Thr
 965 970 975

Met Ile Thr Lys Arg Leu Ala Gln Val Lys Leu Leu Asn Arg Ala Trp
 980 985 990

Arg

<210> 123

<211> 297

<212> PRT

<213> Homo sapiens

<400> 123

Met Ala Lys Val Ser Glu Leu Tyr Asp Val Thr Trp Glu Glu Met Arg
 1 5 10 15

Asp Lys Met Arg Lys Trp Arg Glu Glu Asn Ser Arg Asn Ser Glu Gln
 20 25 30

Ile Val Glu Val Gly Glu Glu Leu Ile Asn Glu Tyr Ala Ser Lys Leu
 35 40 45

Gly Asp Asp Ile Trp Ile Ile Tyr Glu Gln Val Met Ile Ala Ala Leu
 50 55 60

Asp Tyr Gly Arg Asp Asp Leu Ala Leu Phe Cys Leu Gln Glu Leu Arg
 65 70 75 80

Arg Gln Phe Pro Gly Ser His Arg Val Lys Arg Leu Thr Gly Met Arg
 85 90 95

Phe Glu Ala Met Glu Arg Tyr Asp Asp Ala Ile Gln Leu Tyr Asp Arg
 100 105 110

Ile Leu Gln Glu Asp Pro Thr Asn Thr Ala Ala Arg Lys Arg Lys Ile
 115 120 125

Protein Complexes associated with APP-processing

Ala Ile Arg Lys Ala Gln Gly Lys Asn Val Glu Ala Ile Arg Glu Leu
 130 135 140

Asn Glu Tyr Leu Glu Gln Phe Val Gly Asp Gln Glu Ala Trp His Glu
 145 150 155 160

Leu Ala Glu Leu Tyr Ile Asn Glu His Asp Tyr Ala Lys Ala Ala Phe
 165 170 175

Cys Leu Glu Glu Leu Met Met Thr Asn Pro His Asn His Leu Tyr Cys
 180 185 190

Gln Gln Tyr Ala Glu Val Lys Tyr Thr Gln Gly Gly Leu Glu Asn Leu
 195 200 205

Glu Leu Ser Arg Lys Tyr Phe Ala Gln Ala Leu Lys Leu Asn Asn Arg
 210 215 220

Asn Met Arg Ala Leu Phe Gly Leu Tyr Met Ser Ala Ser His Ile Ala
 225 230 235 240

Ser Asn Pro Lys Ala Ser Ala Lys Thr Lys Lys Asp Asn Met Lys Tyr
 245 250 255

Ala Ser Trp Ala Ala Ser Gln Ile Asn Arg Ala Tyr Gln Phe Ala Gly
 260 265 270

Arg Ser Lys Lys Glu Thr Lys Tyr Ser Leu Lys Ala Val Glu Asp Met
 275 280 285

Leu Glu Thr Leu Gln Ile Thr Gln Ser
 290 295

<210> 124

<211> 660

<212> PRT

<213> Homo sapiens

<400> 124

Leu Glu Arg Arg Trp Arg Arg Arg Arg Glu Ala Gly Ala Gly Ala Glu
 1 5 10 15

Ala Ala Ala Gly Ser Ala Arg Pro Leu Gly Arg Gln Ala Ala Ala Ala
 20 25 30

Arg Gly Ser Ser Pro Glu Ala Gly Ala Ala Ala Met Ala Glu Ser Ile
 35 40 45

Protein Complexes associated with APP-processing

Ile Ile Arg Val Gln Ser Pro Asp Gly Val Lys Arg Ile Thr Ala Thr
 50 55 60

Lys Arg Glu Thr Ala Ala Thr Phe Leu Lys Lys Val Ala Lys Glu Phe
 65 70 75 80

Gly Phe Gln Asn Asn Gly Phe Ser Val Tyr Ile Asn Arg Asn Lys Thr
 85 90 95

Gly Glu Ile Thr Ala Ser Ser Asn Lys Ser Leu Asn Leu Leu Lys Ile
 100 105 110

Lys His Gly Asp Leu Leu Phe Leu Phe Pro Ser Ser Leu Ala Gly Pro
 115 120 125

Ser Ser Glu Met Glu Thr Ser Val Pro Pro Gly Phe Lys Val Phe Gly
 130 135 140

Ala Pro Asn Val Val Glu Asp Glu Ile Asp Gln Tyr Leu Ser Lys Gln
 145 150 155 160

Asp Gly Lys Ile Tyr Arg Ser Arg Asp Pro Gln Leu Cys Arg His Gly
 165 170 175

Pro Leu Gly Lys Cys Val His Cys Val Pro Leu Glu Pro Phe Asp Glu
 180 185 190

Asp Tyr Leu Asn His Leu Glu Pro Pro Val Lys His Met Ser Phe His
 195 200 205

Ala Tyr Ile Arg Lys Leu Thr Gly Gly Ala Asp Lys Gly Lys Phe Val
 210 215 220

Ala Leu Glu Asn Ile Ser Cys Lys Ile Lys Ser Gly Cys Glu Gly His
 225 230 235 240

Leu Pro Trp Pro Asn Gly Ile Cys Thr Lys Cys Gln Pro Ser Ala Ile
 245 250 255

Thr Leu Asn Arg Gln Lys Tyr Arg His Val Asp Asn Ile Met Phe Glu
 260 265 270

Asn His Thr Val Ala Asp Arg Phe Leu Asp Phe Trp Arg Lys Thr Gly
 275 280 285

Asn Gln His Phe Gly Tyr Leu Tyr Gly Arg Tyr Thr Glu His Lys Asp
 290 295 300

Ile Pro Leu Gly Ile Arg Ala Glu Val Ala Ala Ile Tyr Glu Pro Pro
 305 310 315 320

Protein Complexes associated with APP-processing
 Gln Ile Gly Thr Gln Asn Ser Leu Glu Leu Leu Glu Asp Pro Lys Ala
 325 330 335

Glu Val Val Asp Glu Ile Ala Ala Lys Leu Gly Leu Arg Lys Val Gly
 340 345 350

Trp Ile Phe Thr Asp Leu Val Ser Glu Asp Thr Arg Lys Gly Thr Val
 355 360 365

Arg Tyr Ser Arg Asn Lys Asp Thr Tyr Phe Leu Ser Ser Glu Glu Cys
 370 375 380

Ile Thr Ala Gly Asp Phe Gln Asn Lys His Pro Asn Met Cys Arg Leu
 385 390 395 400

Ser Pro Asp Gly His Phe Gly Ser Lys Phe Val Thr Ala Val Ala Thr
 405 410 415

Gly Gly Pro Asp Asn Gln Val His Phe Glu Gly Tyr Gln Val Ser Asn
 420 425 430

Gln Cys Met Ala Leu Val Arg Asp Glu Cys Leu Leu Pro Cys Lys Asp
 435 440 445

Ala Pro Glu Leu Gly Tyr Ala Lys Glu Ser Ser Ser Glu Gln Tyr Val
 450 455 460

Pro Asp Val Phe Tyr Lys Asp Val Asp Lys Phe Gly Asn Glu Ile Thr
 465 470 475 480

Gln Leu Ala Arg Pro Leu Pro Val Glu Tyr Leu Ile Ile Asp Ile Thr
 485 490 495

Thr Thr Phe Pro Lys Asp Pro Val Tyr Thr Phe Ser Ile Ser Gln Asn
 500 505 510

Pro Phe Pro Ile Glu Asn Arg Asp Val Leu Gly Glu Thr Gln Asp Phe
 515 520 525

His Ser Leu Ala Thr Tyr Leu Ser Gln Asn Thr Ser Ser Val Phe Leu
 530 535 540

Asp Thr Ile Ser Asp Phe His Leu Leu Leu Phe Leu Val Thr Asn Glu
 545 550 555 560

Val Met Pro Leu Gln Asp Ser Ile Ser Leu Leu Leu Glu Ala Val Arg
 565 570 575

Thr Arg Asn Glu Glu Leu Ala Gln Thr Trp Lys Arg Ser Glu Gln Trp
 580 585 590

Protein Complexes associated with APP-processing
 Ala Thr Ile Glu Gln Leu Cys Ser Glu Tyr Pro His Pro Leu Pro Arg
 595 600 605

His Pro Val Ala Gly Ala Gly Glu Gln Pro Thr Leu His Ser Ser Pro
 610 615 620

Leu Pro Val Val Pro Trp Ile Pro His Pro Ala Ala Ser Trp Gln Val
 625 630 635 640

Pro Ser Ala Met Gln Arg Val Glu Thr Arg Pro Pro Cys Gln Ala Arg
 645 650 655

Gly Arg Leu Arg
 660

<210> 125

<211> 216

<212> PRT

<213> Homo sapiens

<400> 125

Met Trp Ser Ile Gly Ala Gly Ala Leu Gly Ala Ala Ala Leu Ala Leu
 1 5 10 15

Leu Leu Ala Asn Thr Asp Val Phe Leu Ser Lys Pro Gln Lys Ala Ala
 20 25 30

Leu Glu Tyr Leu Glu Asp Ile Asp Leu Lys Thr Leu Glu Lys Glu Pro
 35 40 45

Arg Thr Phe Lys Ala Lys Glu Leu Trp Glu Lys Asn Gly Ala Val Ile
 50 55 60

Met Ala Val Arg Arg Pro Gly Cys Phe Leu Cys Arg Glu Glu Ala Ala
 65 70 75 80

Asp Leu Ser Ser Leu Lys Ser Met Leu Asp Gln Leu Gly Val Pro Leu
 85 90 95

Tyr Ala Val Val Lys Glu His Ile Arg Thr Glu Val Lys Asp Phe Gln
 100 105 110

Pro Tyr Phe Lys Gly Glu Ile Phe Leu Asp Glu Lys Lys Lys Phe Tyr
 115 120 125

Gly Pro Gln Arg Arg Lys Met Met Phe Met Gly Phe Ile Arg Leu Gly
 130 135 140

Protein Complexes associated with APP-processing

Val Trp Tyr Asn Phe Phe Arg Ala Trp Asn Gly Gly Phe Ser Gly Asn
 145 150 155 160

Leu Glu Gly Glu Gly Phe Ile Leu Gly Gly Val Phe Val Val Gly Ser
 165 170 175

Gly Lys Gln Gly Ile Leu Leu Glu His Arg Glu Lys Glu Phe Gly Asp
 180 185 190

Lys Val Asn Leu Leu Ser Val Leu Glu Ala Ala Lys Met Ile Lys Pro
 195 200 205

Gln Thr Leu Ala Ser Glu Lys Lys
 210 215

<210> 126

<211> 253

<212> PRT

<213> Homo sapiens

<400> 126

Met Ala Ser Gly Ser Asn Trp Leu Ser Gly Val Asn Val Val Leu Val
 1 5 10 15

Met Ala Tyr Gly Ser Leu Val Phe Val Leu Leu Phe Ile Phe Val Lys
 20 25 30

Arg Gln Ile Met Arg Phe Ala Met Lys Ser Arg Arg Gly Pro His Val
 35 40 45

Pro Val Gly His Asn Ala Pro Lys Asp Leu Lys Glu Glu Ile Asp Ile
 50 55 60

Arg Leu Ser Arg Val Gln Asp Ile Lys Tyr Glu Pro Gln Leu Leu Ala
 65 70 75 80

Asp Asp Asp Ala Arg Leu Leu Gln Leu Glu Thr Gln Gly Asn Gln Ser
 85 90 95

Cys Tyr Asn Tyr Leu Tyr Arg Met Lys Ala Leu Asp Ala Ile Arg Thr
 100 105 110

Ser Glu Ile Pro Phe His Ser Glu Gly Arg His Pro Arg Ser Leu Met
 115 120 125

Gly Lys Asn Phe Arg Ser Tyr Leu Leu Asp Leu Arg Asn Thr Ser Thr
 130 135 140

Protein Complexes associated with APP-processing

Pro Phe Lys Gly Val Arg Lys Ala Leu Ile Asp Thr Leu Leu Asp Gly
 145 150 155 160

Tyr Glu Thr Ala Arg Tyr Gly Thr Gly Val Phe Gly Gln Asn Glu Tyr
 165 170 175

Leu Arg Tyr Gln Glu Ala Leu Ser Glu Leu Ala Thr Ala Val Lys Ala
 180 185 190

Arg Ile Gly Ser Ser Gln Arg His His Gln Ser Ala Ala Lys Asp Leu
 195 200 205

Thr Gln Ser Pro Glu Val Ser Pro Thr Thr Ile Gln Val Thr Tyr Leu
 210 215 220

Pro Ser Ser Gln Lys Ser Lys Arg Ala Lys His Phe Leu Glu Leu Lys
 225 230 235 240

Ser Phe Lys Asp Asn Tyr Asn Thr Leu Glu Ser Thr Leu
 245 250

<210> 127

<211> 621

<212> PRT

<213> Homo sapiens

<400> 127

Met Ser Gly Cys Gly Leu Phe Leu Arg Thr Thr Ala Ala Ala Arg Ala
 1 5 10 15

Cys Arg Gly Leu Val Val Ser Thr Ala Asn Arg Arg Leu Leu Arg Thr
 20 25 30

Ser Pro Pro Val Arg Ala Phe Ala Lys Glu Leu Phe Leu Gly Lys Ile
 35 40 45

Lys Lys Lys Glu Val Phe Pro Phe Pro Glu Val Ser Gln Asp Glu Leu
 50 55 60

Asn Glu Ile Asn Gln Phe Leu Gly Pro Val Glu Lys Phe Phe Thr Glu
 65 70 75 80

Glu Val Asp Ser Arg Lys Ile Asp Gln Glu Gly Lys Ile Pro Asp Glu
 85 90 95

Thr Leu Glu Lys Leu Lys Ser Leu Gly Leu Phe Gly Leu Gln Val Pro
 100 105 110

Protein Complexes associated with APP-processing

Glu Glu Tyr Gly Gly Leu Gly Phe Ser Asn Thr Met Tyr Ser Arg Leu
 115 120 125

Gly Glu Ile Ile Ser Met Asp Gly Ser Ile Thr Val Thr Leu Ala Ala
 130 135 140

His Gln Ala Ile Gly Leu Lys Gly Ile Ile Leu Ala Gly Thr Glu Glu
 145 150 155 160

Gln Lys Ala Lys Tyr Leu Pro Lys Leu Ala Ser Gly Glu His Ile Ala
 165 170 175

Ala Phe Cys Leu Thr Glu Pro Ala Ser Gly Ser Asp Ala Ala Ser Ile
 180 185 190

Arg Ser Arg Ala Thr Leu Ser Glu Asp Lys Lys His Tyr Ile Leu Asn
 195 200 205

Gly Ser Lys Val Trp Ile Thr Asn Gly Gly Leu Ala Asn Ile Phe Thr
 210 215 220

Val Phe Ala Lys Thr Glu Val Val Asp Ser Asp Gly Ser Val Lys Asp
 225 230 235 240

Lys Ile Thr Ala Phe Ile Val Glu Arg Asp Phe Gly Gly Val Thr Asn
 245 250 255

Gly Lys Pro Glu Asp Lys Leu Gly Ile Arg Gly Ser Asn Thr Cys Glu
 260 265 270

Val His Phe Glu Asn Thr Lys Ile Pro Val Glu Asn Ile Leu Gly Glu
 275 280 285

Val Gly Asp Gly Phe Lys Val Ala Met Asn Ile Leu Asn Ser Gly Arg
 290 295 300

Phe Ser Met Gly Ser Val Val Ala Gly Leu Leu Lys Arg Leu Ile Glu
 305 310 315 320

Met Thr Ala Glu Tyr Ala Cys Thr Arg Lys Gln Phe Asn Lys Arg Leu
 325 330 335

Ser Glu Phe Gly Leu Ile Gln Glu Lys Phe Ala Leu Met Ala Gln Lys
 340 345 350

Ala Tyr Val Met Glu Ser Met Thr Tyr Leu Thr Ala Gly Met Leu Asp
 355 360 365

Gln Pro Gly Phe Pro Asp Cys Ser Ile Glu Ala Ala Met Val Lys Val
 370 375 380

Protein Complexes associated with APP-processing
 Phe Ser Ser Glu Ala Ala Trp Gln Cys Val Ser Glu Ala Leu Gln Ile
 385 390 395 400

Leu Gly Gly Leu Gly Tyr Thr Arg Asp Tyr Pro Tyr Glu Arg Ile Leu
 405 410 415

Arg Asp Thr Arg Ile Leu Leu Ile Phe Glu Gly Thr Asn Glu Ile Leu
 420 425 430

Arg Met Tyr Ile Ala Leu Thr Gly Leu Gln His Ala Gly Arg Ile Leu
 435 440 445

Thr Thr Arg Ile His Glu Leu Lys Gln Ala Lys Val Ser Thr Val Met
 450 455 460

Asp Thr Val Gly Arg Arg Leu Arg Asp Ser Leu Gly Arg Thr Val Asp
 465 470 475 480

Leu Gly Leu Thr Gly Asn His Gly Val Val His Pro Ser Leu Ala Asp
 485 490 495

Ser Ala Asn Lys Phe Glu Glu Asn Thr Tyr Cys Phe Gly Arg Thr Val
 500 505 510

Glu Thr Leu Leu Leu Arg Phe Gly Lys Thr Ile Met Glu Glu Gln Leu
 515 520 525

Val Leu Lys Arg Val Ala Asn Ile Leu Ile Asn Leu Tyr Gly Met Thr
 530 535 540

Ala Val Leu Ser Arg Ala Ser Arg Ser Ile Arg Ile Gly Leu Arg Asn
 545 550 555 560

His Asp His Glu Val Leu Leu Ala Asn Thr Phe Cys Val Glu Ala Tyr
 565 570 575

Leu Gln Asn Leu Phe Ser Leu Ser Gln Leu Asp Lys Tyr Ala Pro Glu
 580 585 590

Asn Leu Asp Glu Gln Ile Lys Lys Val Ser Gln Gln Ile Leu Glu Lys
 595 600 605

Arg Ala Tyr Ile Cys Ala His Pro Leu Asp Arg Thr Cys
 610 615 620

<210> 128

<211> 602

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 128

Met Pro Ser Ala Lys Gln Arg Gly Ser Lys Gly Gly His Gly Ala Ala
 1 5 10 15

Ser Pro Ser Glu Lys Gly Ala His Pro Ser Gly Gly Ala Asp Asp Val
 20 25 30

Ala Lys Lys Pro Pro Pro Ala Pro Gln Gln Pro Pro Pro Pro Ala
 35 40 45

Pro His Pro Gln Gln His Pro Gln Gln His Pro Gln Asn Gln Ala His
 50 55 60

Gly Lys Gly Gly His Arg Gly Gly Gly Gly Gly Gly Gly Lys Ser Ser
 65 70 75 80

Ser Ser Ser Ser Ala Ser Ala Ala Ala Ala Ala Ala Ala Ala Ser Ser
 85 90 95

Ser Ala Ser Cys Ser Arg Arg Leu Gly Arg Ala Leu Asn Phe Leu Phe
 100 105 110

Tyr Leu Ala Leu Val Ala Ala Ala Ala Phe Ser Gly Trp Cys Val His
 115 120 125

His Val Leu Glu Glu Val Gln Gln Val Arg Arg Ser His Gln Asp Phe
 130 135 140

Ser Arg Gln Arg Glu Glu Leu Gly Gln Gly Leu Gln Gly Val Glu Gln
 145 150 155 160

Lys Val Gln Ser Leu Gln Ala Thr Phe Gly Thr Phe Glu Ser Ile Leu
 165 170 175

Arg Ser Ser Gln His Lys Gln Asp Leu Thr Glu Lys Ala Val Lys Gln
 180 185 190

Gly Glu Ser Glu Val Ser Arg Ile Ser Glu Val Leu Gln Lys Leu Gln
 195 200 205

Asn Glu Ile Leu Lys Asp Leu Ser Asp Gly Ile His Val Val Lys Asp
 210 215 220

Ala Arg Glu Arg Asp Phe Thr Ser Leu Glu Asn Thr Val Glu Glu Arg
 225 230 235 240

Leu Thr Glu Leu Thr Lys Ser Ile Asn Asp Asn Ile Ala Ile Phe Thr
 245 250 255

Protein Complexes associated with APP-processing

Leu Leu Ser Gln Asp Gln Ala Gln Ala Ala Arg Leu Pro Pro Gln Asp
515 520 525

Protein Complexes associated with APP-processing

Phe Leu Asp Arg Leu Ser Ser Leu Asp Asn Leu Lys Ala Ser Val Ser
 530 535 540

Gln Val Glu Ala Asp Leu Lys Met Leu Arg Thr Ala Val Asp Ser Leu
 545 550 555 560

Val Ala Tyr Ser Val Lys Ile Glu Thr Asn Glu Asn Asn Leu Glu Ser
 565 570 575

Ala Lys Gly Leu Leu Asp Asp Leu Arg Asn Asp Leu Asp Arg Leu Phe
 580 585 590

Val Lys Val Glu Lys Ile His Glu Lys Val
 595 600

<210> 129

<211> 263

<212> PRT

<213> Homo sapiens

<400> 129

Met Phe Arg Asn Gln Tyr Asp Asn Asp Val Thr Val Trp Ser Pro Gln
 1 5 10 15

Gly Arg Ile His Gln Ile Glu Tyr Ala Met Glu Ala Val Lys Gln Gly
 20 25 30

Ser Ala Thr Val Gly Leu Lys Ser Lys Thr His Ala Val Leu Val Ala
 35 40 45

Leu Lys Arg Ala Gln Ser Glu Leu Ala Ala His Gln Lys Lys Ile Leu
 50 55 60

His Val Asp Asn His Ile Gly Ile Ser Ile Ala Gly Leu Thr Ala Asp
 65 70 75 80

Ala Arg Leu Leu Cys Asn Phe Met Arg Gln Glu Cys Leu Asp Ser Arg
 85 90 95

Phe Val Phe Asp Arg Pro Leu Pro Val Ser Arg Leu Val Ser Leu Ile
 100 105 110

Gly Ser Lys Thr Gln Ile Pro Thr Gln Arg Tyr Gly Arg Arg Pro Tyr
 115 120 125

Gly Val Gly Leu Leu Ile Ala Gly Tyr Asp Asp Met Gly Pro His Ile
 130 135 140

Protein Complexes associated with APP-processing
 Phe Gln Thr Cys Pro Ser Ala Asn Tyr Phe Asp Cys Arg Ala Met Ser
 145 150 155 160

Ile Gly Ala Arg Ser Gln Ser Ala Arg Thr Tyr Leu Glu Arg His Met
 165 170 175

Ser Glu Phe Met Glu Cys Asn Leu Asn Glu Leu Val Lys His Gly Leu
 180 185 190

Arg Ala Leu Arg Glu Thr Leu Pro Ala Glu Gln Asp Leu Thr Thr Lys
 195 200 205

Asn Val Ser Ile Gly Ile Val Gly Lys Asp Leu Glu Phe Thr Ile Tyr
 210 215 220

Asp Asp Asp Asp Val Ser Pro Phe Leu Glu Gly Leu Glu Glu Arg Pro
 225 230 235 240

Gln Arg Lys Ala Gln Pro Ala Gln Pro Ala Asp Glu Pro Ala Glu Lys
 245 250 255

Ala Asp Glu Pro Met Glu His
 260

<210> 130

<211> 254

<212> PRT

<213> Homo sapiens

<400> 130

Ser Ser Ile Gly Thr Gly Tyr Asp Leu Ser Ala Ser Thr Phe Ser Pro
 1 5 10 15

Asp Gly Arg Val Phe Gln Val Glu Tyr Ala Met Lys Ala Val Glu Asn
 20 25 30

Ser Ser Thr Ala Ile Gly Ile Arg Cys Lys Asp Gly Val Val Phe Gly
 35 40 45

Val Glu Lys Leu Val Leu Ser Lys Leu Tyr Glu Glu Gly Ser Asn Lys
 50 55 60

Arg Leu Phe Asn Val Asp Arg His Val Gly Met Ala Val Ala Gly Leu
 65 70 75 80

Leu Ala Asp Ala Arg Ser Leu Ala Asp Ile Ala Arg Glu Glu Ala Ser
 85 90 95

Protein Complexes associated with APP-processing

Asn Phe Arg Ser Asn Phe Gly Tyr Asn Ile Pro Leu Lys His Leu Ala
 100 105 110

Asp Arg Val Ala Met Tyr Val His Ala Tyr Thr Leu Tyr Ser Ala Val
 115 120 125

Arg Pro Phe Gly Cys Ser Phe Met Leu Gly Ser Tyr Ser Val Asn Asp
 130 135 140

Gly Ala Gln Leu Tyr Met Ile Asp Pro Ser Gly Val Ser Tyr Gly Tyr
 145 150 155 160

Trp Gly Cys Ala Ile Gly Lys Ala Arg Gln Ala Ala Lys Thr Glu Ile
 165 170 175

Glu Lys Leu Gln Met Lys Glu Met Thr Cys Arg Asp Ile Val Lys Glu
 180 185 190

Val Ala Lys Ile Ile Tyr Ile Val His Asp Glu Val Lys Asp Lys Ala
 195 200 205

Phe Glu Leu Glu Leu Ser Trp Val Gly Glu Leu Thr Asn Gly Arg His
 210 215 220

Glu Ile Val Pro Lys Asp Ile Arg Glu Glu Ala Glu Lys Tyr Ala Lys
 225 230 235 240

Glu Ser Leu Lys Glu Glu Asp Glu Ser Asp Asp Asp Asn Met
 245 250

<210> 131

<211> 261

<212> PRT

<213> Homo sapiens

<400> 131

Met Ser Arg Arg Tyr Asp Ser Arg Thr Thr Ile Phe Ser Pro Glu Gly
 1 5 10 15

Arg Leu Tyr Gln Val Glu Tyr Ala Met Glu Ala Ile Gly His Ala Gly
 20 25 30

Thr Cys Leu Gly Ile Leu Ala Asn Asp Gly Val Leu Leu Ala Ala Glu
 35 40 45

Arg Arg Asn Ile His Lys Leu Leu Asp Glu Val Phe Phe Ser Glu Lys
 50 55 60

Protein Complexes associated with APP-processing

Ile Tyr Lys Leu Asn Glu Asp Met Ala Cys Ser Val Ala Gly Ile Thr
65 70 75 80

Ser Asp Ala Asn Val Leu Thr Asn Glu Leu Arg Leu Ile Ala Gln Arg
85 90 95

Tyr Leu Leu Gln Tyr Gln Glu Pro Ile Pro Cys Glu Gln Leu Val Thr
100 105 110

Ala Leu Cys Asp Ile Lys Gln Ala Tyr Thr Gln Phe Gly Gly Lys Arg
115 120 125

Pro Phe Gly Val Ser Leu Leu Tyr Ile Gly Trp Asp Lys His Tyr Gly
130 135 140

Phe Gln Leu Tyr Gln Ser Asp Pro Ser Gly Asn Tyr Gly Gly Trp Lys
145 150 155 160

Ala Thr Cys Ile Gly Asn Asn Ser Ala Ala Ala Val Ser Met Leu Lys
165 170 175

Gln Asp Tyr Lys Glu Gly Glu Met Thr Leu Lys Ser Ala Leu Ala Leu
180 185 190

Ala Ile Lys Val Leu Asn Lys Thr Met Asp Val Ser Lys Leu Ser Ala
195 200 205

Glu Lys Val Glu Ile Ala Thr Leu Thr Arg Glu Asn Gly Lys Thr Val
210 215 220

Ile Arg Val Leu Lys Gln Lys Glu Val Glu Gln Leu Ile Lys Lys His
225 230 235 240

Glu Glu Glu Glu Ala Lys Ala Glu Arg Glu Lys Lys Glu Lys Glu Gln
245 250 255

Lys Glu Lys Asp Lys
260

<210> 132

<211> 246

<212> PRT

<213> Homo sapiens

<400> 132

Met Ser Arg Gly Ser Ser Ala Gly Phe Asp Arg His Ile Thr Ile Phe
1 5 10 15

Protein Complexes associated with APP-processing

Ser Pro Glu Gly Arg Leu Tyr Gln Val Glu Tyr Ala Phe Lys Ala Ile
 20 25 30

Asn Gln Gly Gly Leu Thr Ser Val Ala Val Arg Gly Lys Asp Cys Ala
 35 40 45

Val Ile Val Thr Gln Lys Lys Val Pro Asp Lys Leu Leu Asp Ser Ser
 50 55 60

Thr Val Thr His Leu Phe Lys Ile Thr Glu Asn Ile Gly Cys Val Met
 65 70 75 80

Thr Gly Met Thr Ala Asp Ser Arg Ser Gln Val Gln Arg Ala Arg Tyr
 85 90 95

Glu Ala Ala Asn Trp Lys Tyr Lys Tyr Gly Tyr Glu Ile Pro Val Asp
 100 105 110

Met Leu Cys Lys Arg Ile Ala Asp Ile Ser Gln Val Tyr Thr Gln Asn
 115 120 125

Ala Glu Met Arg Pro Leu Gly Cys Cys Met Ile Leu Ile Gly Ile Asp
 130 135 140

Glu Glu Gln Gly Pro Gln Val Tyr Lys Cys Asp Pro Ala Gly Tyr Tyr
 145 150 155 160

Cys Gly Phe Lys Ala Thr Ala Ala Gly Val Lys Gln Thr Glu Ser Thr
 165 170 175

Ser Phe Leu Glu Lys Lys Val Lys Lys Lys Phe Asp Trp Thr Phe Glu
 180 185 190

Gln Thr Val Glu Thr Ala Ile Thr Cys Leu Ser Thr Val Leu Ser Ile
 195 200 205

Asp Phe Lys Pro Ser Glu Ile Glu Val Gly Val Val Thr Val Glu Asn
 210 215 220

Pro Lys Phe Arg Ile Leu Thr Glu Ala Glu Ile Asp Ala His Leu Val
 225 230 235 240

Ala Leu Ala Glu Arg Asp
 245

<210> 133

<211> 241

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 133

Met Leu Ser Ser Thr Ala Met Tyr Ser Ala Pro Gly Arg Asp Leu Gly
 1 5 10 15

Met Glu Pro His Arg Ala Ala Gly Pro Leu Gln Leu Arg Phe Ser Pro
 20 25 30

Tyr Val Phe Asn Gly Gly Thr Ile Leu Ala Ile Ala Gly Glu Asp Phe
 35 40 45

Ala Ile Val Ala Ser Asp Thr Arg Leu Ser Glu Gly Phe Ser Ile His
 50 55 60

Thr Arg Asp Ser Pro Lys Cys Tyr Lys Leu Thr Asp Lys Thr Val Ile
 65 70 75 80

Gly Cys Ser Gly Phe His Gly Asp Cys Leu Thr Leu Thr Lys Ile Ile
 85 90 95

Glu Ala Arg Leu Lys Met Tyr Lys His Ser Asn Asn Lys Ala Met Thr
 100 105 110

Thr Gly Ala Ile Ala Ala Met Leu Ser Thr Ile Leu Tyr Ser Arg Arg
 115 120 125

Phe Phe Pro Tyr Tyr Val Tyr Asn Ile Ile Gly Gly Leu Asp Glu Glu
 130 135 140

Gly Lys Gly Ala Val Tyr Ser Phe Asp Pro Val Gly Ser Tyr Gln Arg
 145 150 155 160

Asp Ser Phe Lys Ala Gly Gly Ser Ala Ser Ala Met Leu Gln Pro Leu
 165 170 175

Leu Asp Asn Gln Val Gly Phe Lys Asn Met Gln Asn Val Glu His Val
 180 185 190

Pro Leu Ser Leu Asp Arg Ala Met Arg Leu Val Lys Asp Val Phe Ile
 195 200 205

Ser Ala Ala Glu Arg Asp Val Tyr Thr Gly Asp Ala Leu Arg Ile Cys
 210 215 220

Ile Val Thr Lys Glu Gly Ile Arg Glu Glu Thr Val Ser Leu Arg Lys
 225 230 235 240

Asp

Protein Complexes associated with APP-processing

<210> 134

<211> 201

<212> PRT

<213> Homo sapiens

<400> 134

Met Glu Tyr Leu Ile Gly Ile Gln Gly Pro Asp Tyr Val Leu Val Ala
 1 5 10 15

Ser Asp Arg Val Ala Ala Ser Asn Ile Val Gln Met Lys Asp Asp His
 20 25 30

Asp Lys Met Phe Lys Met Ser Glu Lys Ile Leu Leu Leu Cys Val Gly
 35 40 45

Glu Ala Gly Asp Thr Val Gln Phe Ala Glu Tyr Ile Gln Lys Asn Val
 50 55 60

Gln Leu Tyr Lys Met Arg Asn Gly Tyr Glu Leu Ser Pro Thr Ala Ala
 65 70 75 80

Ala Asn Phe Thr Arg Arg Asn Leu Ala Asp Cys Leu Arg Ser Arg Thr
 85 90 95

Pro Tyr His Val Asn Leu Leu Leu Ala Gly Tyr Asp Glu His Glu Gly
 100 105 110

Pro Ala Leu Tyr Tyr Met Asp Tyr Leu Ala Ala Leu Ala Lys Ala Pro
 115 120 125

Phe Ala Ala His Gly Tyr Gly Ala Phe Leu Thr Leu Ser Ile Leu Asp
 130 135 140

Arg Tyr Tyr Thr Pro Thr Ile Ser Arg Glu Arg Ala Val Glu Leu Leu
 145 150 155 160

Arg Lys Cys Leu Glu Glu Leu Gln Lys Arg Phe Ile Leu Asn Leu Pro
 165 170 175

Thr Phe Ser Val Arg Ile Ile Asp Lys Asn Gly Ile His Asp Leu Asp
 180 185 190

Asn Ile Ser Phe Pro Lys Gln Gly Ser
 195 200

<210> 135

<211> 205

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 135

Met Ser Ile Met Ser Tyr Asn Gly Gly Ala Val Met Ala Met Lys Gly
 1 5 10 15

Lys Asn Cys Val Ala Ile Ala Ala Asp Arg Arg Phe Gly Ile Gln Ala
 20 25 30

Gln Met Val Thr Thr Asp Phe Gln Lys Ile Phe Pro Met Gly Asp Arg
 35 40 45

Leu Tyr Ile Gly Leu Ala Gly Leu Ala Thr Asp Val Gln Thr Val Ala
 50 55 60

Gln Arg Leu Lys Phe Arg Leu Asn Leu Tyr Glu Leu Lys Glu Gly Arg
 65 70 75 80

Gln Ile Lys Pro Tyr Thr Leu Met Ser Met Val Ala Asn Leu Leu Tyr
 85 90 95

Glu Lys Arg Phe Gly Pro Tyr Tyr Thr Glu Pro Val Ile Ala Gly Leu
 100 105 110

Asp Pro Lys Thr Phe Lys Pro Phe Ile Cys Ser Leu Asp Leu Ile Gly
 115 120 125

Cys Pro Met Val Thr Asp Asp Phe Val Val Ser Gly Thr Cys Ala Glu
 130 135 140

Gln Met Tyr Gly Met Cys Glu Ser Leu Trp Glu Pro Asn Met Asp Pro
 145 150 155 160

Asp His Leu Phe Glu Thr Ile Ser Gln Ala Met Leu Asn Ala Val Asp
 165 170 175

Arg Asp Ala Val Ser Gly Met Gly Val Ile Val His Ile Ile Glu Lys
 180 185 190

Asp Lys Ile Thr Thr Arg Thr Leu Lys Ala Arg Met Asp
 195 200 205

<210> 136

<211> 264

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 136

Met Glu Ala Phe Leu Gly Ser Arg Ser Gly Leu Trp Ala Gly Gly Pro
 1 5 10 15

Ala Pro Gly Gln Phe Tyr Arg Ile Pro Ser Thr Pro Asp Ser Phe Met
 20 25 30

Asp Pro Ala Ser Ala Leu Tyr Arg Gly Pro Ile Thr Arg Thr Gln Asn
 35 40 45

Pro Met Val Thr Gly Thr Ser Val Leu Gly Val Lys Phe Glu Gly Gly
 50 55 60

Val Val Ile Ala Ala Asp Met Leu Gly Ser Tyr Gly Ser Leu Ala Arg
 65 70 75 80

Phe Arg Asn Ile Ser Arg Ile Met Arg Val Asn Asn Ser Thr Met Leu
 85 90 95

Gly Ala Ser Gly Asp Tyr Ala Asp Phe Gln Tyr Leu Lys Gln Val Leu
 100 105 110

Gly Gln Met Val Ile Asp Glu Glu Leu Leu Gly Asp Gly His Ser Tyr
 115 120 125

Ser Pro Arg Ala Ile His Ser Trp Leu Thr Arg Ala Met Tyr Ser Arg
 130 135 140

Arg Ser Lys Met Asn Pro Leu Trp Asn Thr Met Val Ile Gly Gly Tyr
 145 150 155 160

Ala Asp Gly Glu Ser Phe Leu Gly Tyr Val Asp Met Leu Gly Val Ala
 165 170 175

Tyr Glu Ala Pro Ser Leu Ala Thr Gly Tyr Gly Ala Tyr Leu Ala Gln
 180 185 190

Pro Leu Leu Arg Glu Val Leu Glu Lys Gln Pro Val Leu Ser Gln Thr
 195 200 205

Glu Ala Arg Asp Leu Val Glu Arg Cys Met Arg Val Leu Tyr Tyr Arg
 210 215 220

Asp Ala Arg Ser Tyr Asn Arg Phe Gln Thr Ala Thr Val Thr Glu Lys
 225 230 235 240

Gly Val Glu Ile Glu Gly Pro Leu Ser Thr Glu Thr Asn Trp Asp Ile
 245 250 255

Protein Complexes associated with APP-processing
 Ala His Met Ile Ser Gly Phe Glu
 260

<210> 137

<211> 208

<212> PRT

<213> Homo sapiens

<400> 137

Met Leu His Gly Thr Thr Thr Leu Ala Phe Lys Phe Arg His Gly Val
 1 5 10 15

Ile Val Ala Ala Asp Ser Arg Ala Thr Ala Gly Ala Tyr Ile Ala Ser
 20 25 30

Gln Thr Val Lys Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr
 35 40 45

Met Ala Gly Gly Ala Ala Asp Cys Ser Phe Trp Glu Arg Leu Leu Ala
 50 55 60

Arg Gln Cys Arg Ile Tyr Glu Leu Arg Asn Lys Glu Arg Ile Ser Val
 65 70 75 80

Ala Ala Ala Ser Lys Leu Leu Ala Asn Met Val Tyr Gln Tyr Lys Gly
 85 90 95

Met Gly Leu Ser Met Gly Thr Met Ile Cys Gly Trp Asp Lys Arg Gly
 100 105 110

Pro Gly Leu Tyr Tyr Val Asp Ser Glu Gly Asn Arg Ile Ser Gly Ala
 115 120 125

Thr Phe Ser Val Gly Ser Gly Ser Val Tyr Ala Tyr Gly Val Met Asp
 130 135 140

Arg Tyr Ser Tyr Asp Leu Glu Val Glu Gln Ala Tyr Asp Leu Ala
 145 150 155 160

Arg Arg a Ile Tyr Gln Ala Thr Tyr Arg Asp Ala Tyr Ser Gly Gly
 165 170 175

Ala Val Asn Leu r His Val Arg Glu Asp Gly Trp Ile Arg Val Ser
 180 185 190

Ser Asp Asn Val Ala sp Leu His Glu Lys Tyr Ser Gly Ser Thr Pro
 195 200 205

Protein Complexes associated with APP-processing

<210> 138

<211> 239

<212> PRT

<213> Homo sapiens

<400> 138

Met Ala Ala Thr Leu Leu Ala Ala Arg Gly Ala Gly Pro Ala Pro Ala
 1 5 10 15

Trp Gly Pro Glu Ala Phe Thr Pro Asp Trp Glu Ser Arg Glu Val Ser
 20 25 30

Thr Gly Thr Thr Ile Met Ala Val Gln Phe Asp Gly Gly Val Val Leu
 35 40 45

Gly Ala Asp Ser Arg Thr Thr Thr Gly Ser Tyr Ile Ala Asn Arg Val
 50 55 60

Thr Asp Lys Leu Thr Pro Ile His Asp Arg Ile Phe Cys Cys Arg Ser
 65 70 75 80

Gly Ser Ala Ala Asp Thr Gln Ala Val Ala Asp Ala Val Thr Tyr Gln
 85 90 95

Leu Gly Phe His Ser Ile Glu Leu Asn Glu Pro Pro Leu Val His Thr
 100 105 110

Ala Ala Ser Leu Phe Lys Glu Met Cys Tyr Arg Tyr Arg Glu Asp Leu
 115 120 125

Met Ala Gly Ile Ile Ile Ala Gly Trp Asp Pro Gln Glu Gly Gly Gln
 130 135 140

Val Tyr Ser Val Pro Met Gly Gly Met Met Val Arg Gln Ser Phe Ala
 145 150 155 160

Ile Gly Gly Ser Gly Ser Ser Tyr Ile Tyr Gly Tyr Val Asp Ala Thr
 165 170 175

Tyr Arg Glu Gly Met Thr Lys Glu Glu Cys Leu Gln Phe Thr Ala Asn
 180 185 190

Ala Leu Ala Leu Ala Met Glu Arg Asp Gly Ser Ser Gly Gly Val Ile
 195 200 205

Arg Leu Ala Ala Ile Ala Glu Ser Gly Val Glu Arg Gln Val Leu Leu
 210 215 220

Protein Complexes associated with APP-processing
 Gly Asp Gln Ile Pro Lys Phe Ala Val Ala Thr Leu Pro Pro Ala
 225 230 235

<210> 139

<211> 440

<212> PRT

<213> Homo sapiens

<400> 139

Met Gly Gln Ser Gln Ser Gly Gly His Gly Pro Gly Gly Gly Lys Lys
 1 5 10 15

Asp Asp Lys Asp Lys Lys Lys Lys Tyr Glu Pro Pro Val Pro Thr Arg
 20 25 30

Val Gly Lys Lys Lys Lys Lys Thr Lys Gly Pro Asp Ala Ala Ser Lys
 35 40 45

Leu Pro Leu Val Thr Pro His Thr Gln Cys Arg Leu Lys Leu Leu Lys
 50 55 60

Leu Glu Arg Ile Lys Asp Tyr Leu Leu Met Glu Glu Glu Phe Ile Arg
 65 70 75 80

Asn Gln Glu Gln Met Lys Pro Leu Glu Glu Lys Gln Glu Glu Glu Arg
 85 90 95

Ser Lys Val Asp Asp Leu Arg Gly Thr Pro Met Ser Val Gly Thr Leu
 100 105 110

Glu Glu Ile Ile Asp Asp Asn His Ala Ile Val Ser Thr Ser Val Gly
 115 120 125

Ser Glu His Tyr Val Ser Ile Leu Ser Phe Val Asp Lys Asp Leu Leu
 130 135 140

Glu Pro Gly Cys Ser Val Leu Leu Asn His Lys Val His Ala Val Ile
 145 150 155 160

Gly Val Leu Met Asp Asp Thr Asp Pro Leu Val Thr Val Met Lys Val
 165 170 175

Glu Lys Ala Pro Gln Glu Thr Tyr Ala Asp Ile Gly Gly Leu Asp Asn
 180 185 190

Gln Ile Gln Glu Ile Lys Glu Ser Val Glu Leu Pro Leu Thr His Pro
 195 200 205

Protein Complexes associated with APP-processing
 Glu Tyr Tyr Glu Glu Met Gly Ile Lys Pro Pro Lys Gly Val Ile Leu
 210 215 220

Tyr Gly Pro Pro Gly Thr Gly Lys Thr Leu Leu Ala Lys Ala Val Ala
 225 230 235 240

Asn Gln Thr Ser Ala Thr Phe Leu Arg Val Val Gly Ser Glu Leu Ile
 245 250 255

Gln Lys Tyr Leu Gly Asp Gly Pro Lys Leu Val Arg Glu Leu Phe Arg
 260 265 270

Val Ala Glu Glu His Ala Pro Ser Ile Val Phe Ile Asp Glu Ile Asp
 275 280 285

Ala Ile Gly Thr Lys Arg Tyr Asp Ser Asn Ser Gly Gly Glu Arg Glu
 290 295 300

Ile Gln Arg Thr Met Leu Glu Leu Leu Asn Gln Leu Asp Gly Phe Asp
 305 310 315 320

Ser Arg Gly Asp Val Lys Val Ile Met Ala Thr Asn Arg Ile Glu Thr
 325 330 335

Leu Asp Pro Ala Leu Ile Arg Pro Gly Arg Ile Asp Arg Lys Ile Glu
 340 345 350

Phe Pro Leu Pro Asp Glu Lys Thr Lys Lys Arg Ile Phe Gln Ile His
 355 360 365

Thr Ser Arg Met Thr Leu Ala Asp Asp Val Thr Leu Asp Asp Leu Ile
 370 375 380

Met Ala Lys Asp Asp Leu Ser Gly Ala Asp Ile Lys Ala Ile Cys Thr
 385 390 395 400

Glu Ala Gly Leu Met Ala Leu Arg Glu Arg Arg Met Lys Val Thr Asn
 405 410 415

Glu Asp Phe Lys Lys Ser Lys Glu Asn Val Leu Tyr Lys Lys Gln Glu
 420 425 430

Gly Thr Pro Glu Gly Leu Tyr Leu
 435 440

<210> 140

<211> 433

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 140

Met Pro Asp Tyr Leu Gly Ala Asp Gln Arg Lys Thr Lys Glu Asp Glu
 1 5 10 15

Lys Asp Asp Lys Pro Ile Arg Ala Leu Asp Glu Gly Asp Ile Ala Leu
 20 25 30

Leu Lys Thr Tyr Gly Gln Ser Thr Tyr Ser Arg Gln Ile Lys Gln Val
 35 40 45

Glu Asp Asp Ile Gln Gln Leu Leu Lys Lys Ile Asn Glu Leu Thr Gly
 50 55 60

Ile Lys Glu Ser Asp Thr Gly Leu Ala Pro Pro Ala Leu Trp Asp Leu
 65 70 75 80

Ala Ala Asp Lys Gln Thr Leu Gln Ser Glu Gln Pro Leu Gln Val Ala
 85 90 95

Arg Cys Thr Lys Ile Ile Asn Ala Asp Ser Glu Asp Pro Lys Tyr Ile
 100 105 110

Ile Asn Val Lys Gln Phe Ala Lys Phe Val Val Asp Leu Ser Asp Gln
 115 120 125

Val Ala Pro Thr Asp Ile Glu Glu Gly Met Arg Val Gly Val Asp Arg
 130 135 140

Asn Lys Tyr Gln Ile His Ile Pro Leu Pro Pro Lys Ile Asp Pro Thr
 145 150 155 160

Val Thr Met Met Gln Val Glu Glu Lys Pro Asp Val Thr Tyr Ser Asp
 165 170 175

Val Gly Gly Cys Lys Glu Gln Ile Glu Lys Leu Arg Glu Val Val Glu
 180 185 190

Thr Pro Leu Leu His Pro Glu Arg Phe Val Asn Leu Gly Ile Glu Pro
 195 200 205

Pro Lys Gly Val Leu Leu Phe Gly Pro Pro Gly Thr Gly Lys Thr Leu
 210 215 220

Cys Ala Arg Ala Val Ala Asn Arg Thr Asp Ala Cys Phe Ile Arg Val
 225 230 235 240

Ile Gly Ser Glu Leu Val Gln Lys Tyr Val Gly Glu Gly Ala Arg Met
 245 250 255

Protein Complexes associated with APP-processing

Val Arg Glu Leu Phe Glu Met Ala Arg Thr Lys Lys Ala Cys Leu Ile
 260 265 270

Phe Phe Asp Glu Ile Asp Ala Ile Gly Gly Ala Arg Phe Asp Asp Gly
 275 280 285

Ala Gly Gly Asp Asn Glu Val Gln Arg Thr Met Leu Glu Leu Ile Asn
 290 295 300

Gln Leu Asp Gly Phe Asp Pro Arg Gly Asn Ile Lys Val Leu Met Ala
 305 310 315 320

Thr Asn Arg Pro Asp Thr Leu Asp Pro Ala Leu Met Arg Pro Gly Arg
 325 330 335

Leu Asp Arg Lys Ile Glu Phe Ser Leu Pro Asp Leu Glu Gly Arg Thr
 340 345 350

His Ile Phe Lys Ile His Ala Arg Ser Met Ser Val Glu Arg Asp Ile
 355 360 365

Arg Phe Glu Leu Leu Ala Arg Leu Cys Pro Asn Ser Thr Gly Ala Glu
 370 375 380

Ile Arg Ser Val Cys Thr Glu Ala Gly Met Phe Ala Ile Arg Ala Arg
 385 390 395 400

Arg Lys Ile Ala Thr Glu Lys Asp Phe Leu Glu Ala Val Asn Lys Val
 405 410 415

Ile Lys Ser Tyr Ala Lys Phe Ser Ala Thr Pro Arg Tyr Met Thr Tyr
 420 425 430

Asn

<210> 141

<211> 439

<212> PRT

<213> Homo sapiens

<400> 141

Met Asn Leu Leu Pro Asn Ile Glu Ser Pro Val Thr Arg Gln Glu Lys
 1 5 10 15

Met Ala Thr Val Trp Asp Glu Ala Glu Gln Asp Gly Ile Gly Glu Glu
 20 25 30

Protein Complexes associated with APP-processing

Val Leu Lys Met Ser Thr Glu Glu Ile Ile Gln Arg Thr Arg Leu Leu
 35 40 45

Asp Ser Glu Ile Lys Ile Met Lys Ser Glu Val Leu Arg Val Thr His
 50 55 60

Glu Leu Gln Ala Met Lys Asp Lys Ile Lys Glu Asn Ser Glu Lys Ile
 65 70 75 80

Lys Val Asn Lys Thr Leu Pro Tyr Leu Val Ser Asn Val Ile Glu Leu
 85 90 95

Leu Asp Val Asp Pro Asn Asp Gln Glu Glu Asp Gly Ala Asn Ile Asp
 100 105 110

Leu Asp Ser Gln Arg Lys Gly Lys Cys Ala Val Ile Lys Thr Ser Thr
 115 120 125

Arg Gln Thr Tyr Phe Leu Pro Val Ile Gly Leu Val Asp Ala Glu Lys
 130 135 140

Leu Lys Pro Gly Asp Leu Val Gly Val Asn Lys Asp Ser Tyr Leu Ile
 145 150 155 160

Leu Glu Thr Leu Pro Thr Glu Tyr Asp Ser Arg Val Lys Ala Met Glu
 165 170 175

Val Asp Glu Arg Pro Thr Glu Gln Tyr Ser Asp Ile Gly Gly Leu Asp
 180 185 190

Lys Gln Ile Gln Glu Leu Val Glu Ala Ile Val Leu Pro Met Asn His
 195 200 205

Lys Glu Lys Phe Glu Asn Leu Gly Ile Gln Pro Pro Lys Gly Val Leu
 210 215 220

Met Tyr Gly Pro Pro Gly Thr Gly Lys Thr Leu Leu Ala Arg Ala Cys
 225 230 235 240

Ala Ala Gln Thr Lys Ala Thr Phe Leu Lys Leu Ala Gly Pro Gln Leu
 245 250 255

Val Gln Met Phe Ile Gly Asp Gly Ala Lys Leu Val Arg Asp Ala Phe
 260 265 270

Ala Leu Ala Lys Glu Lys Ala Pro Ser Ile Ile Phe Ile Asp Glu Leu
 275 280 285

Asp Ala Ile Gly Thr Lys Arg Phe Asp Ser Glu Lys Ala Gly Asp Arg
 290 295 300

Protein Complexes associated with APP-processing

Glu Val Gln Arg Thr Met Leu Glu Leu Leu Asn Gln Leu Asp Gly Phe
 305 310 315 320

Gln Pro Asn Thr Gln Val Lys Val Ile Ala Ala Thr Asn Arg Val Asp
 325 330 335

Ile Leu Asp Pro Ala Leu Leu Arg Ser Gly Arg Leu Asp Arg Lys Ile
 340 345 350

Glu Phe Pro Met Pro Asn Glu Glu Ala Arg Ala Arg Ile Met Gln Ile
 355 360 365

His Ser Arg Lys Met Asn Val Ser Pro Asp Val Asn Tyr Glu Glu Leu
 370 375 380

Ala Arg Cys Thr Asp Asp Phe Asn Gly Ala Gln Cys Lys Ala Val Cys
 385 390 395 400

Val Glu Ala Gly Met Ile Ala Leu Arg Arg Gly Ala Thr Glu Leu Thr
 405 410 415

His Glu Asp Tyr Met Glu Gly Ile Leu Glu Val Gln Ala Lys Lys Lys
 420 425 430

Ala Asn Leu Gln Tyr Tyr Ala
 435

<210> 142

<211> 418

<212> PRT

<213> Homo sapiens

<400> 142

Met Glu Glu Ile Gly Ile Leu Val Glu Lys Ala Gln Asp Glu Ile Pro
 1 5 10 15

Ala Leu Ser Val Ser Arg Pro Gln Thr Gly Leu Ser Phe Leu Gly Pro
 20 25 30

Glu Pro Glu Asp Leu Glu Asp Leu Tyr Ser Arg Tyr Lys Lys Leu Gln
 35 40 45

Gln Glu Leu Glu Phe Leu Glu Val Gln Glu Glu Tyr Ile Lys Asp Glu
 50 55 60

Gln Lys Asn Leu Lys Lys Glu Phe Leu His Ala Gln Glu Glu Val Lys
 65 70 75 80

Protein Complexes associated with APP-processing

Arg Ile Gln Ser Ile Pro Leu Val Ile Gly Gln Phe Leu Glu Ala Val
85 90 95

Asp Gln Asn Thr Ala Ile Val Gly Ser Thr Thr Gly Ser Asn Tyr Tyr
100 105 110

Val Arg Ile Leu Ser Thr Ile Asp Arg Glu Leu Leu Lys Pro Asn Ala
115 120 125

Ser Val Ala Leu His Lys His Ser Asn Ala Leu Val Asp Val Leu Pro
130 135 140

Pro Glu Ala Asp Ser Ser Ile Met Met Leu Thr Ser Asp Gln Lys Pro
145 150 155 160

Asp Val Met Tyr Ala Asp Ile Gly Gly Met Asp Ile Gln Lys Gln Glu
165 170 175

Val Arg Glu Ala Val Glu Leu Pro Leu Thr His Phe Glu Leu Tyr Lys
180 185 190

Gln Ile Gly Ile Asp Pro Pro Arg Gly Val Leu Met Tyr Gly Pro Pro
195 200 205

Gly Cys Gly Lys Thr Met Leu Ala Lys Ala Val Ala His His Thr Thr
210 215 220

Ala Ala Phe Ile Arg Val Val Gly Ser Glu Phe Val Gln Lys Tyr Leu
225 230 235 240

Gly Glu Gly Pro Arg Met Val Arg Asp Val Phe Arg Leu Ala Lys Glu
245 250 255

Asn Ala Pro Ala Ile Ile Phe Ile Asp Glu Ile Asp Ala Ile Ala Thr
260 265 270

Lys Arg Phe Asp Ala Gln Thr Gly Ala Asp Arg Glu Val Gln Arg Ile
275 280 285

Leu Leu Glu Leu Leu Asn Gln Met Asp Gly Phe Asp Gln Asn Val Asn
290 295 300

Val Lys Val Ile Met Ala Thr Asn Arg Ala Asp Thr Leu Asp Pro Ala
305 310 315 320

Leu Leu Arg Pro Gly Arg Leu Asp Arg Lys Ile Glu Phe Pro Leu Pro
325 330 335

Asp Arg Arg Gln Lys Arg Leu Ile Phe Ser Thr Ile Thr Ser Lys Met
340 345 350

Protein Complexes associated with APP-processing
 Asn Leu Ser Glu Glu Val Asp Leu Glu Asp Tyr Val Ala Arg Pro Asp
 355 360 365

Lys Ile Ser Gly Ala Asp Ile Asn Ser Ile Cys Gln Glu Ser Gly Met
 370 375 380

Leu Ala Val Arg Glu Asn Arg Tyr Ile Val Leu Ala Lys Asp Phe Glu
 385 390 395 400

Lys Ala Tyr Lys Thr Val Ile Lys Lys Asp Glu Gln Glu His Glu Phe
 405 410 415

Tyr Lys

<210> 143

<211> 406

<212> PRT

<213> Homo sapiens

<400> 143

Met Ala Leu Asp Gly Pro Glu Gln Met Glu Leu Glu Glu Gly Lys Ala
 1 5 10 15

Gly Ser Gly Leu Arg Gln Tyr Tyr Leu Ser Lys Ile Glu Glu Leu Gln
 20 25 30

Leu Ile Val Asn Asp Lys Ser Gln Asn Leu Arg Arg Leu Gln Ala Gln
 35 40 45

Arg Asn Glu Leu Asn Ala Lys Val Arg Leu Leu Arg Glu Glu Leu Gln
 50 55 60

Leu Leu Gln Glu Gln Gly Ser Tyr Val Gly Glu Val Val Arg Ala Met
 65 70 75 80

Asp Lys Lys Lys Val Leu Val Lys Val His Pro Glu Gly Lys Phe Val
 85 90 95

Val Asp Val Asp Lys Asn Ile Asp Ile Asn Asp Val Thr Pro Asn Cys
 100 105 110

Arg Val Ala Leu Arg Asn Asp Ser Tyr Thr Leu His Lys Ile Leu Pro
 115 120 125

Asn Lys Val Asp Pro Leu Val Ser Leu Met Met Val Glu Lys Val Pro
 130 135 140

Protein Complexes associated with APP-processing

Asp Ser Thr Tyr Glu Met Ile Gly Gly Leu Asp Lys Gln Ile Lys Glu
 145 150 155 160

Ile Lys Glu Val Ile Glu Leu Pro Val Lys His Pro Glu Leu Phe Glu
 165 170 175

Ala Leu Gly Ile Ala Gln Pro Lys Gly Val Leu Leu Tyr Gly Pro Pro
 180 185 190

Gly Thr Gly Lys Thr Leu Leu Ala Arg Ala Val Ala His His Thr Asp
 195 200 205

Cys Thr Phe Ile Arg Val Ser Gly Ser Glu Leu Val Gln Lys Phe Ile
 210 215 220

Gly Glu Gly Ala Arg Met Val Arg Glu Leu Phe Val Met Ala Arg Glu
 225 230 235 240

His Ala Pro Ser Ile Ile Phe Met Asp Glu Ile Asp Ser Ile Gly Ser
 245 250 255

Ser Arg Leu Glu Gly Gly Ser Gly Gly Asp Ser Glu Val Gln Arg Thr
 260 265 270

Met Leu Glu Leu Leu Asn Gln Leu Asp Gly Phe Glu Ala Thr Lys Asn
 275 280 285

Ile Lys Val Ile Met Ala Thr Asn Arg Ile Asp Ile Leu Asp Ser Ala
 290 295 300

Leu Leu Arg Pro Gly Arg Ile Asp Arg Lys Ile Glu Phe Pro Pro Pro
 305 310 315 320

Asn Glu Glu Ala Arg Leu Asp Ile Leu Lys Ile His Ser Arg Lys Met
 325 330 335

Asn Leu Thr Arg Gly Ile Asn Leu Arg Lys Ile Ala Glu Leu Met Pro
 340 345 350

Gly Ala Ser Gly Ala Glu Val Lys Gly Val Cys Thr Glu Ala Gly Met
 355 360 365

Tyr Ala Leu Arg Glu Arg Arg Val His Val Thr Gln Glu Asp Phe Glu
 370 375 380

Met Ala Val Ala Lys Val Met Gln Lys Asp Ser Glu Lys Asn Met Ser
 385 390 395 400

Ile Lys Lys Leu Trp Lys
 405

Protein Complexes associated with APP-processing

<210> 144

<211> 389

<212> PRT

<213> Homo sapiens

<400> 144

Met Ala Asp Pro Arg Asp Lys Ala Leu Gln Asp Tyr Arg Lys Lys Leu
 1 5 10 15

Leu Glu His Lys Glu Ile Asp Gly Arg Leu Lys Glu Leu Arg Glu Gln
 20 25 30

Leu Lys Glu Leu Thr Lys Gln Tyr Glu Lys Ser Glu Asn Asp Leu Lys
 35 40 45

Ala Leu Gln Ser Val Gly Gln Ile Val Gly Glu Val Leu Lys Gln Leu
 50 55 60

Thr Glu Glu Lys Phe Ile Val Lys Ala Thr Asn Gly Pro Arg Tyr Val
 65 70 75 80

Val Gly Cys Arg Arg Gln Leu Asp Lys Ser Lys Leu Lys Pro Gly Thr
 85 90 95

Arg Val Ala Leu Asp Met Thr Thr Leu Thr Ile Met Arg Tyr Leu Pro
 100 105 110

Arg Glu Val Asp Pro Leu Val Tyr Asn Met Ser His Glu Asp Pro Gly
 115 120 125

Asn Val Ser Tyr Ser Glu Ile Gly Gly Leu Ser Glu Gln Ile Arg Glu
 130 135 140

Leu Arg Glu Val Ile Glu Leu Pro Leu Thr Asn Pro Glu Leu Phe Gln
 145 150 155 160

Arg Val Gly Ile Ile Pro Pro Lys Gly Cys Leu Leu Tyr Gly Pro Pro
 165 170 175

Gly Thr Gly Lys Thr Leu Leu Ala Arg Ala Val Ala Ser Gln Leu Asp
 180 185 190

Cys Asn Phe Leu Lys Val Val Ser Ser Ser Ile Val Asp Lys Tyr Ile
 195 200 205

Gly Glu Ser Ala Arg Leu Ile Arg Glu Met Phe Asn Tyr Ala Arg Asp
 210 215 220

Protein Complexes associated with APP-processing
 His Gln Pro Cys Ile Ile Phe Met Asp Glu Ile Asp Ala Ile Gly Gly
 225 230 235 240

Arg Arg Phe Ser Glu Gly Thr Ser Ala Asp Arg Glu Ile Gln Arg Thr
 245 250 255

Leu Met Glu Leu Leu Asn Gln Met Asp Gly Phe Asp Thr Leu His Arg
 260 265 270

Val Lys Met Ile Met Ala Thr Asn Arg Pro Asp Thr Leu Asp Pro Ala
 275 280 285

Leu Leu Arg Pro Gly Arg Leu Asp Arg Lys Ile His Ile Asp Leu Pro
 290 295 300

Asn Glu Gln Ala Arg Leu Asp Ile Leu Lys Ile His Ala Gly Pro Ile
 305 310 315 320

Thr Lys His Gly Glu Ile Asp Tyr Glu Ala Ile Val Lys Leu Ser Asp
 325 330 335

Gly Phe Asn Gly Ala Asp Leu Arg Asn Val Cys Thr Glu Ala Gly Met
 340 345 350

Phe Ala Ile Arg Ala Asp His Asp Phe Val Val Gln Glu Asp Phe Met
 355 360 365

Lys Ala Val Arg Lys Val Ala Asp Ser Lys Lys Leu Glu Ser Lys Leu
 370 375 380

Asp Tyr Lys Pro Val
 385

<210> 145

<211> 389

<212> PRT

<213> Homo sapiens

<400> 145

Met Ala Asp Pro Arg Asp Lys Ala Leu Gln Asp Tyr Arg Lys Lys Leu
 1 5 10 15

Leu Glu His Lys Glu Ile Asp Gly Arg Leu Lys Glu Leu Arg Glu Gln
 20 25 30

Leu Lys Glu Leu Thr Lys Gln Tyr Glu Lys Ser Glu Asn Asp Leu Lys
 35 40 45

Protein Complexes associated with APP-processing

Ala Leu Gln Ser Val Gly Gln Ile Val Gly Glu Val Leu Lys Gln Leu
 50 55 60

Thr Glu Glu Lys Phe Ile Val Lys Ala Thr Asn Gly Pro Arg Tyr Val
 65 70 75 80

Val Gly Cys Arg Arg Gln Leu Asp Lys Ser Lys Leu Lys Pro Gly Thr
 85 90 95

Arg Val Ala Leu Asp Met Thr Thr Leu Thr Ile Met Arg Tyr Leu Pro
 100 105 110

Arg Glu Val Asp Pro Leu Val Tyr Asn Met Ser His Glu Asp Pro Gly
 115 120 125

Asn Val Ser Tyr Ser Glu Ile Gly Gly Leu Ser Glu Gln Ile Arg Glu
 130 135 140

Leu Arg Glu Val Ile Glu Leu Pro Leu Thr Asn Pro Glu Leu Phe Gln
 145 150 155 160

Arg Val Gly Ile Ile Pro Pro Lys Gly Cys Leu Leu Tyr Gly Pro Pro
 165 170 175

Gly Thr Gly Lys Thr Leu Leu Ala Arg Ala Val Ala Ser Gln Leu Asp
 180 185 190

Cys Asn Phe Leu Lys Val Val Ser Ser Ser Ile Val Asp Lys Tyr Ile
 195 200 205

Gly Glu Ser Ala Arg Leu Ile Arg Glu Met Phe Asn Tyr Ala Arg Asp
 210 215 220

His Gln Pro Cys Ile Ile Phe Met Asp Glu Ile Asp Ala Ile Gly Gly
 225 230 235 240

Arg Arg Phe Ser Glu Gly Thr Ser Ala Asp Arg Glu Ile Gln Arg Thr
 245 250 255

Leu Met Glu Leu Leu Asn Gln Met Asp Gly Phe Asp Thr Leu His Arg
 260 265 270

Val Lys Met Ile Met Ala Thr Asn Arg Pro Asp Thr Leu Asp Pro Ala
 275 280 285

Leu Leu Arg Pro Gly Arg Leu Asp Arg Lys Ile His Ile Asp Leu Pro
 290 295 300

Asn Glu Gln Ala Arg Leu Asp Ile Leu Lys Ile His Ala Gly Pro Ile
 305 310 315 320

Protein Complexes associated with APP-processing
 Thr Lys His Gly Glu Ile Asp Tyr Glu Ala Ile Val Lys Leu Ser Asp
 325 330 335

Gly Phe Asn Gly Ala Asp Leu Arg Asn Val Cys Thr Glu Ala Gly Met
 340 345 350

Phe Ala Ile Arg Ala Asp His Asp Phe Val Val Gln Glu Asp Phe Met
 355 360 365

Lys Ala Val Arg Lys Val Ala Asp Ser Lys Lys Leu Glu Ser Lys Leu
 370 375 380

Asp Tyr Lys Pro Val
 385

<210> 146

<211> 422

<212> PRT

<213> Homo sapiens

<400> 146

Met Ala Ala Ala Ala Val Val Glu Phe Gln Arg Ala Gln Ser Leu Leu
 1 5 10 15

Ser Thr Asp Arg Glu Ala Ser Ile Asp Ile Leu His Ser Ile Val Lys
 20 25 30

Arg Asp Ile Gln Glu Asn Asp Glu Glu Ala Val Gln Val Lys Glu Gln
 35 40 45

Ser Ile Leu Glu Leu Gly Ser Leu Leu Ala Lys Thr Gly Gln Ala Ala
 50 55 60

Glu Leu Gly Gly Leu Leu Lys Tyr Val Arg Pro Phe Leu Asn Ser Ile
 65 70 75 80

Ser Lys Ala Lys Ala Ala Arg Leu Val Arg Ser Leu Leu Asp Leu Phe
 85 90 95

Leu Asp Met Glu Ala Ala Thr Gly Gln Glu Val Glu Leu Cys Leu Glu
 100 105 110

Cys Ile Glu Trp Ala Lys Ser Glu Lys Arg Thr Phe Leu Arg Gln Ala
 115 120 125

Leu Glu Ala Arg Leu Val Ser Leu Tyr Phe Asp Thr Lys Arg Tyr Gln
 130 135 140

Protein Complexes associated with APP-processing

Glu Ala Leu His Leu Gly Ser Gln Leu Leu Arg Glu Leu Lys Lys Met
 145 150 155 160

Asp Asp Lys Ala Leu Leu Val Glu Val Gln Leu Leu Glu Ser Lys Thr
 165 170 175

Tyr His Ala Leu Ser Asn Leu Pro Lys Ala Arg Ala Ala Leu Thr Ser
 180 185 190

Ala Arg Thr Thr Ala Asn Ala Ile Tyr Cys Pro Pro Lys Leu Gln Ala
 195 200 205

Thr Leu Asp Met Gln Ser Gly Ile Ile His Ala Ala Glu Glu Lys Asp
 210 215 220

Trp Lys Thr Ala Tyr Ser Tyr Phe Tyr Glu Ala Phe Glu Gly Tyr Asp
 225 230 235 240

Ser Ile Asp Ser Pro Lys Ala Ile Thr Ser Leu Lys Tyr Met Leu Leu
 245 250 255

Cys Lys Ile Met Leu Asn Thr Pro Glu Asp Val Gln Ala Leu Val Ser
 260 265 270

Gly Lys Leu Ala Leu Arg Tyr Ala Gly Arg Gln Thr Glu Ala Leu Lys
 275 280 285

Cys Val Ala Gln Ala Ser Lys Asn Arg Ser Leu Ala Asp Phe Glu Lys
 290 295 300

Ala Leu Thr Asp Tyr Arg Ala Glu Leu Arg Asp Asp Pro Ile Ile Ser
 305 310 315 320

Thr His Leu Ala Lys Leu Tyr Asp Asn Leu Leu Glu Gln Asn Leu Ile
 325 330 335

Arg Val Ile Glu Pro Phe Ser Arg Val Gln Ile Glu His Ile Ser Ser
 340 345 350

Leu Ile Lys Leu Ser Lys Ala Asp Val Glu Arg Lys Leu Ser Gln Met
 355 360 365

Ile Leu Asp Lys Lys Phe His Gly Ile Leu Asp Gln Gly Glu Gly Val
 370 375 380

Leu Ile Ile Phe Asp Glu Pro Pro Val Asp Lys Thr Tyr Glu Ala Ala
 385 390 395 400

Leu Glu Thr Ile Gln Asn Met Ser Lys Val Val Asp Ser Leu Tyr Asn
 405 410 415

Protein Complexes associated with APP-processing
 Lys Ala Lys Lys Leu Thr
 420

<210> 147

<211> 456

<212> PRT

<213> Homo sapiens

<400> 147

Met Ala Asp Gly Gly Ser Glu Arg Ala Asp Gly Arg Ile Val Lys Met
 1 5 10 15

Glu Val Asp Tyr Ser Ala Thr Val Asp Gln Arg Leu Pro Glu Cys Ala
 20 25 30

Lys Leu Ala Lys Glu Gly Arg Leu Gln Glu Val Ile Glu Thr Leu Leu
 35 40 45

Ser Leu Glu Lys Gln Thr Arg Thr Ala Ser Asp Met Val Ser Thr Ser
 50 55 60

Arg Ile Leu Val Ala Val Val Lys Met Cys Tyr Glu Ala Lys Glu Trp
 65 70 75 80

Asp Leu Leu Asn Glu Asn Ile Met Leu Leu Ser Lys Arg Arg Ser Gln
 85 90 95

Leu Lys Gln Ala Val Ala Lys Met Val Gln Gln Cys Cys Thr Tyr Val
 100 105 110

Glu Glu Ile Thr Asp Leu Pro Ile Lys Leu Arg Leu Ile Asp Thr Leu
 115 120 125

Arg Met Val Thr Glu Gly Lys Ile Tyr Val Glu Ile Glu Arg Ala Arg
 130 135 140

Leu Thr Lys Thr Leu Ala Thr Ile Lys Glu Gln Asn Gly Asp Val Lys
 145 150 155 160

Glu Ala Ala Ser Ile Leu Gln Glu Leu Gln Val Glu Thr Tyr Gly Ser
 165 170 175

Met Glu Lys Lys Glu Arg Val Glu Phe Ile Leu Glu Gln Met Arg Leu
 180 185 190

Cys Leu Ala Val Lys Asp Tyr Ile Arg Thr Gln Ile Ile Ser Lys Lys
 195 200 205

Protein Complexes associated with APP-processing

Ile Asn Thr Lys Phe Phe Gln Glu Glu Asn Thr Glu Lys Leu Lys Leu
 210 215 220

Lys Tyr Tyr Asn Leu Met Ile Gln Leu Asp Gln His Glu Gly Ser Tyr
 225 230 235 240

Leu Ser Ile Cys Lys His Tyr Arg Ala Ile Tyr Asp Thr Pro Cys Ile
 245 250 255

Gln Ala Glu Ser Glu Lys Trp Gln Gln Ala Leu Lys Ser Val Val Leu
 260 265 270

Tyr Val Ile Leu Ala Pro Phe Asp Asn Glu Gln Ser Asp Leu Val His
 275 280 285

Arg Ile Ser Gly Asp Lys Lys Leu Glu Glu Ile Pro Lys Tyr Lys Asp
 290 295 300

Leu Leu Lys Leu Phe Thr Thr Met Glu Leu Met Arg Trp Ser Thr Leu
 305 310 315 320

Val Glu Asp Tyr Gly Met Glu Leu Arg Lys Gly Ser Leu Glu Ser Pro
 325 330 335

Ala Thr Asp Val Phe Gly Ser Thr Glu Glu Gly Glu Lys Arg Trp Lys
 340 345 350

Asp Leu Lys Asn Arg Val Val Glu His Asn Ile Arg Ile Met Ala Lys
 355 360 365

Tyr Tyr Thr Arg Ile Thr Met Lys Arg Met Ala Gln Leu Leu Asp Leu
 370 375 380

Ser Val Asp Glu Ser Glu Ala Phe Leu Ser Asn Leu Val Val Asn Lys
 385 390 395 400

Thr Ile Phe Ala Lys Val Asp Arg Leu Ala Gly Ile Ile Asn Phe Gln
 405 410 415

Arg Pro Lys Asp Pro Asn Asn Leu Leu Asn Asp Trp Ser Gln Lys Leu
 420 425 430

Asn Ser Leu Met Ser Leu Val Asn Lys Thr Thr His Leu Ile Ala Lys
 435 440 445

Glu Glu Met Ile His Asn Leu Gln
 450 455

<210> 148

<211> 376

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 148

Met Lys Asp Val Pro Gly Phe Leu Gln Gln Ser Gln Asn Ser Gly Pro
 1 5 10 15

Gly Gln Pro Ala Val Trp His Arg Leu Glu Glu Leu Tyr Thr Lys Lys
 20 25 30

Leu Trp His Gln Leu Thr Leu Gln Val Leu Asp Phe Val Gln Asp Pro
 35 40 45

Cys Phe Ala Gln Gly Asp Gly Leu Ile Lys Leu Tyr Glu Asn Phe Ile
 50 55 60

Ser Glu Phe Glu His Arg Val Asn Pro Leu Ser Leu Val Glu Ile Ile
 65 70 75 80

Leu His Val Val Arg Gln Met Thr Asp Pro Asn Val Ala Leu Thr Phe
 85 90 95

Leu Glu Lys Thr Arg Glu Lys Val Lys Ser Ser Asp Glu Ala Val Ile
 100 105 110

Leu Cys Lys Thr Ala Ile Gly Ala Leu Lys Leu Asn Ile Gly Asp Leu
 115 120 125

Gln Val Thr Lys Glu Thr Ile Glu Asp Val Glu Glu Met Leu Asn Asn
 130 135 140

Leu Pro Gly Val Thr Ser Val His Ser Arg Phe Tyr Asp Leu Ser Ser
 145 150 155 160

Lys Tyr Tyr Gln Thr Ile Gly Asn His Ala Ser Tyr Tyr Lys Asp Ala
 165 170 175

Leu Arg Phe Leu Gly Cys Val Asp Ile Lys Asp Leu Pro Val Ser Glu
 180 185 190

Gln Gln Glu Arg Ala Phe Thr Leu Gly Leu Ala Gly Leu Leu Gly Glu
 195 200 205

Gly Val Phe Asn Phe Gly Glu Leu Leu Met His Pro Val Leu Glu Ser
 210 215 220

Leu Arg Asn Thr Asp Arg Gln Trp Leu Ile Asp Thr Leu Tyr Ala Phe
 225 230 235 240

Protein Complexes associated with APP-processing

Protein Complexes associated with APP-processing

Gln Ile Arg Ser Ser Thr Thr Ser Met Thr Ser Val Pro Lys Pro Leu
85 90 95

Lys Phe Leu Arg Pro His Tyr Gly Lys Leu Lys Glu Ile Tyr Glu Asn
100 105 110

Met Ala Pro Gly Glu Asn Lys Arg Phe Ala Ala Asp Ile Ile Ser Val
115 120 125

Leu Ala Met Thr Met Ser Gly Glu Arg Glu Cys Leu Lys Tyr Arg Leu
130 135 140

Val Gly Ser Gln Glu Glu Leu Ala Ser Trp Gly His Glu Tyr Val Arg
145 150 155 160

His Leu Ala Gly Glu Val Ala Lys Glu Trp Gln Glu Leu Asp Asp Ala
165 170 175

Glu Lys Val Gln Arg Glu Pro Leu Leu Thr Leu Val Lys Glu Ile Val
180 185 190

Pro Tyr Asn Met Ala His Asn Ala Glu His Glu Ala Cys Asp Leu Leu
195 200 205

Met Glu Ile Glu Gln Val Asp Met Leu Glu Lys Asp Ile Asp Glu Asn
210 215 220

Ala Tyr Ala Lys Val Cys Leu Tyr Leu Thr Ser Cys Val Asn Tyr Val
225 230 235 240

Pro Glu Pro Glu Asn Ser Ala Leu Leu Arg Cys Ala Leu Gly Val Phe
245 250 255

Arg Lys Phe Ser Arg Phe Pro Glu Ala Leu Arg Leu Ala Leu Met Leu
260 265 270

Asn Asp Met Glu Leu Val Glu Asp Ile Phe Thr Ser Cys Lys Asp Val
275 280 285

Val Val Gln Lys Gln Met Ala Phe Met Leu Gly Arg His Gly Val Phe
290 295 300

Leu Glu Leu Ser Glu Asp Val Glu Glu Tyr Glu Asp Leu Thr Glu Ile
305 310 315 320

Met Ser Asn Val Gln Leu Asn Ser Asn Phe Leu Ala Leu Ala Arg Glu
325 330 335

Leu Asp Ile Met Glu Pro Lys Val Pro Asp Asp Ile Tyr Lys Thr His
340 345 350

Protein Complexes associated with APP-processing

Leu Glu Asn Asn Arg Phe Gly Gly Ser Gly Ser Gln Val Asp Ser Ala
 355 360 365

Arg Met Asn Leu Ala Ser Ser Phe Val Asn Gly Phe Val Asn Ala Ala
 370 375 380

Phe Gly Gln Asp Lys Leu Leu Thr Asp Asp Gly Asn Lys Trp Leu Tyr
 385 390 395 400

Lys Asn Lys Asp His Gly Met Leu Ser Ala Ala Ala Ser Leu Gly Met
 405 410 415

Ile Leu Leu Trp Asp Val Asp Gly Gly Leu Thr Gln Ile Asp Lys Tyr
 420 425 430

Leu Tyr Ser Ser Glu Asp Tyr Ile Lys Ser Gly Ala Leu Leu Ala Cys
 435 440 445

Gly Ile Val Asn Ser Gly Val Arg Asn Glu Cys Asp Pro Ala Leu Ala
 450 455 460

Leu Leu Ser Asp Tyr Val Leu His Asn Ser Asn Thr Met Arg Leu Gly
 465 470 475 480

Ser Ile Phe Gly Leu Gly Leu Ala Tyr Ala Gly Ser Asn Arg Glu Asp
 485 490 495

Val Leu Thr Leu Leu Leu Pro Val Met Gly Asp Ser Lys Ser Ser Met
 500 505 510

Glu Val Ala Gly Val Thr Ala Leu Ala Cys Gly Met Ile Ala Val Gly
 515 520 525

Ser Cys Asn Gly Asp Val Thr Ser Thr Ile Leu Gln Thr Ile Met Glu
 530 535 540

Lys Ser Glu Thr Glu Leu Lys Asp Thr Tyr Ala Arg Trp Leu Pro Leu
 545 550 555 560

Gly Leu Gly Leu Asn His Leu Gly Lys Gly Glu Ala Ile Glu Ala Ile
 565 570 575

Leu Ala Ala Leu Glu Val Val Ser Glu Pro Phe Arg Ser Phe Ala Asn
 580 585 590

Thr Leu Val Asp Val Cys Ala Tyr Ala Gly Ser Gly Asn Val Leu Lys
 595 600 605

Val Gln Gln Leu Leu His Ile Cys Ser Glu His Phe Asp Ser Lys Glu
 610 615 620

Protein Complexes associated with APP-processing

Lys Glu Glu Asp Lys Asp Lys Lys Glu Lys Lys Asp Lys Asp Lys Lys
 625 630 635 640

Glu Ala Pro Ala Asp Met Gly Ala His Gln Gly Val Ala Val Leu Gly
 645 650 655

Ile Ala Leu Ile Ala Met Gly Glu Glu Ile Gly Ala Glu Met Ala Leu
 660 665 670

Arg Thr Phe Gly His Leu Leu Arg Tyr Gly Glu Pro Thr Leu Arg Arg
 675 680 685

Ala Val Pro Leu Ala Leu Ala Leu Ile Ser Val Ser Asn Pro Arg Leu
 690 695 700

Asn Ile Leu Asp Thr Leu Ser Lys Phe Ser His Asp Ala Asp Pro Glu
 705 710 715 720

Val Ser Tyr Asn Ser Ile Phe Ala Met Gly Met Val Gly Ser Gly Thr
 725 730 735

Asn Asn Ala Arg Leu Ala Ala Met Leu Arg Gln Leu Ala Gln Tyr His
 740 745 750

Ala Lys Asp Pro Asn Asn Leu Phe Met Val Arg Leu Ala Gln Gly Leu
 755 760 765

Thr His Leu Gly Lys Gly Thr Leu Thr Leu Cys Pro Tyr His Ser Asp
 770 775 780

Arg Gln Leu Met Ser Gln Val Ala Val Ala Gly Leu Leu Thr Val Leu
 785 790 795 800

Val Ser Phe Leu Asp Val Arg Asn Ile Ile Leu Gly Lys Ser His Tyr
 805 810 815

Val Leu Tyr Gly Leu Val Ala Ala Met Gln Pro Arg Met Leu Val Thr
 820 825 830

Phe Asp Glu Glu Leu Arg Pro Leu Pro Val Ser Val Arg Val Gly Gln
 835 840 845

Ala Val Asp Val Val Gly Gln Ala Gly Lys Pro Lys Thr Ile Thr Gly
 850 855 860

Phe Gln Thr His Thr Thr Pro Val Leu Leu Ala His Gly Glu Arg Ala
 865 870 875 880

Glu Leu Ala Thr Glu Glu Phe Leu Pro Val Thr Pro Ile Leu Glu Gly
 885 890 895

Protein Complexes associated with APP-processing
 Phe Val Ile Leu Arg Lys Asn Pro Asn Tyr Asp Leu
 900 905

<210> 150

<211> 534

<212> PRT

<213> Homo sapiens

<400> 150

Met Lys Gln Glu Gly Ser Ala Arg Arg Arg Gly Ala Asp Lys Ala Lys
 1 5 10 15

Pro Pro Pro Gly Gly Gly Glu Gln Glu Pro Pro Pro Pro Pro Ala Pro
 20 25 30

Gln Asp Val Glu Met Lys Glu Glu Ala Ala Thr Gly Gly Gly Ser Thr
 35 40 45

Gly Glu Ala Asp Gly Lys Thr Ala Ala Ala Ala Ala Glu His Ser Gln
 50 55 60

Arg Glu Leu Asp Thr Val Thr Leu Glu Asp Ile Lys Glu His Val Lys
 65 70 75 80

Gln Leu Glu Lys Ala Val Ser Gly Lys Glu Pro Arg Phe Val Leu Arg
 85 90 95

Ala Leu Arg Met Leu Pro Ser Thr Ser Arg Arg Leu Asn His Tyr Val
 100 105 110

Leu Tyr Lys Ala Val Gln Gly Phe Phe Thr Ser Asn Asn Ala Thr Arg
 115 120 125

Asp Phe Leu Leu Pro Phe Leu Glu Glu Pro Met Asp Thr Glu Ala Asp
 130 135 140

Leu Gln Phe Arg Pro Arg Thr Gly Lys Ala Ala Ser Thr Pro Leu Leu
 145 150 155 160

Pro Glu Val Glu Ala Tyr Leu Gln Leu Leu Val Val Ile Phe Met Met
 165 170 175

Asn Ser Lys Arg Tyr Lys Glu Ala Gln Lys Ile Ser Asp Asp Leu Met
 180 185 190

Gln Lys Ile Ser Thr Gln Asn Arg Arg Ala Leu Asp Leu Val Ala Ala
 195 200 205

Protein Complexes associated with APP-processing

Lys Cys Tyr Tyr Tyr His Ala Arg Val Tyr Glu Phe Leu Asp Lys Leu
 210 215 220

Asp Val Val Arg Ser Phe Leu His Ala Arg Leu Arg Thr Ala Thr Leu
 225 230 235 240

Arg His Asp Ala Asp Gly Gln Ala Thr Leu Leu Asn Leu Leu Leu Arg
 245 250 255

Asn Tyr Leu His Tyr Ser Leu Tyr Asp Gln Ala Glu Lys Leu Val Ser
 260 265 270

Lys Ser Val Phe Pro Glu Gln Ala Asn Asn Asn Glu Trp Ala Arg Tyr
 275 280 285

Leu Tyr Tyr Thr Gly Arg Ile Lys Ala Ile Gln Leu Glu Tyr Ser Glu
 290 295 300

Ala Arg Arg Thr Met Thr Asn Ala Leu Arg Lys Ala Pro Gln His Thr
 305 310 315 320

Ala Val Gly Phe Lys Gln Thr Val His Lys Leu Leu Ile Val Val Glu
 325 330 335

Leu Leu Leu Gly Glu Ile Pro Asp Arg Leu Gln Phe Arg Gln Pro Ser
 340 345 350

Leu Lys Arg Ser Leu Met Pro Tyr Phe Leu Leu Thr Gln Ala Val Arg
 355 360 365

Thr Gly Asn Leu Ala Lys Phe Asn Gln Val Leu Asp Gln Phe Gly Glu
 370 375 380

Lys Phe Gln Ala Asp Gly Thr Tyr Thr Leu Ile Ile Arg Leu Arg His
 385 390 395 400

Asn Val Ile Lys Thr Gly Val Arg Met Ile Ser Leu Ser Tyr Ser Arg
 405 410 415

Ile Ser Leu Ala Asp Ile Ala Gln Lys Leu Gln Leu Asp Ser Pro Glu
 420 425 430

Asp Ala Glu Phe Ile Val Ala Lys Ala Ile Arg Asp Gly Val Ile Glu
 435 440 445

Ala Ser Ile Asn His Glu Lys Gly Tyr Val Gln Ser Lys Glu Met Ile
 450 455 460

Asp Ile Tyr Ser Thr Arg Glu Pro Gln Leu Ala Phe His Gln Arg Ile
 465 470 475 480

Protein Complexes associated with APP-processing

Ser Phe Cys Leu Asp Ile His Asn Met Ser Val Lys Ala Met Arg Phe
 485 490 495

Pro Pro Lys Ser Tyr Asn Lys Asp Leu Glu Ser Ala Glu Glu Arg Arg
 500 505 510

Glu Arg Glu Gln Gln Asp Leu Glu Phe Ala Lys Glu Met Ala Glu Asp
 515 520 525

Asp Asp Asp Ser Phe Pro
 530

<210> 151

<211> 377

<212> PRT

<213> Homo sapiens

<400> 151

Met Val Leu Glu Ser Thr Met Val Cys Val Asp Asn Ser Glu Tyr Met
 1 5 10 15

Arg Asn Gly Asp Phe Leu Pro Thr Arg Leu Gln Ala Gln Gln Asp Ala
 20 25 30

Val Asn Ile Val Cys His Ser Lys Thr Arg Ser Asn Pro Glu Asn Asn
 35 40 45

Val Gly Leu Ile Thr Leu Ala Asn Asp Cys Glu Val Leu Thr Thr Leu
 50 55 60

Thr Pro Asp Thr Gly Arg Ile Leu Ser Lys Leu His Thr Val Gln Pro
 65 70 75 80

Lys Gly Lys Ile Thr Phe Cys Thr Gly Ile Arg Val Ala His Leu Ala
 85 90 95

Leu Lys His Arg Gln Gly Lys Asn His Lys Met Arg Ile Ile Ala Phe
 100 105 110

Val Gly Ser Pro Val Glu Asp Asn Glu Lys Asp Leu Val Lys Leu Ala
 115 120 125

Lys Arg Leu Lys Lys Glu Lys Val Asn Val Asp Ile Ile Asn Phe Gly
 130 135 140

Glu Glu Glu Val Asn Thr Glu Lys Leu Thr Ala Phe Val Asn Thr Leu
 145 150 155 160

Protein Complexes associated with APP-processing

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Protein Complexes associated with APP-processing

Met Leu Thr Phe Met Ala Ser Asp Ser Glu Glu Glu Val Cys Asp Glu
 1 5 10 15

Arg Thr Ser Leu Met Ser Ala Glu Ser Pro Thr Pro Arg Ser Cys Gln
 20 25 30

Glu Gly Arg Gln Gly Pro Glu Asp Gly Glu Asn Thr Ala Gln Trp Arg
 35 40 45

Ser Gln Glu Asn Glu Glu Asp Gly Glu Glu Asp Pro Asp Arg Tyr Val
 50 55 60

Cys Ser Gly Val Pro Gly Arg Pro Pro Gly Leu Glu Glu Glu Leu Thr
 65 70 75 80

Leu Lys Tyr Gly Ala Lys His Val Ile Met Leu Phe Val Pro Val Thr
 85 90 95

Leu Cys Met Ile Val Val Val Ala Thr Ile Lys Ser Val Arg Phe Tyr
 100 105 110

Thr Glu Lys Asn Gly Gln Leu Ile Tyr Thr Pro Phe Thr Glu Asp Thr
 115 120 125

Pro Ser Val Gly Gln Arg Leu Leu Asn Ser Val Leu Asn Thr Leu Ile
 130 135 140

Met Ile Ser Val Ile Val Val Met Thr Ile Phe Leu Val Val Leu Tyr
 145 150 155 160

Lys Tyr Arg Cys Tyr Lys Phe Ile His Gly Trp Leu Ile Met Ser Ser
 165 170 175

Leu Met Leu Leu Phe Leu Phe Thr Tyr Ile Tyr Leu Gly Glu Val Leu
 180 185 190

Lys Thr Tyr Asn Val Ala Met Asp Tyr Pro Thr Leu Leu Leu Thr Val
 195 200 205

Trp Asn Phe Gly Ala Val Gly Met Val Cys Ile His Trp Lys Gly Pro
 210 215 220

Leu Val Leu Gln Gln Ala Tyr Leu Ile Met Ile Ser Ala Leu Met Ala
 225 230 235 240

Leu Val Phe Ile Lys Tyr Leu Pro Glu Trp Ser Ala Trp Val Ile Leu
 245 250 255

Gly Ala Ile Ser Val Tyr Asp Leu Val Ala Val Leu Cys Pro Lys Gly
 260 265 270

Protein Complexes associated with APP-processing
 Pro Leu Arg Met Leu Val Glu Thr Ala Gln Glu Arg Asn Glu Pro Ile
 275 280 285

Phe Pro Ala Leu Ile Tyr Ser Ser Ala Met Val Trp Thr Val Gly Met
 290 295 300

Ala Lys Leu Asp Pro Ser Ser Gln Gly Ala Leu Gln Leu Pro Tyr Asp
 305 310 315 320

Pro Glu Met Glu Glu Asp Ser Tyr Asp Ser Phe Gly Glu Pro Ser Tyr
 325 330 335

Pro Glu Val Phe Glu Pro Pro Leu Thr Gly Tyr Pro Gly Glu Glu Leu
 340 345 350

Glu Glu Glu Glu Glu Arg Gly Val Lys Leu Gly Leu Gly Asp Phe Ile
 355 360 365

Phe Tyr Ser Val Leu Val Gly Lys Ala Ala Ala Thr Gly Ser Gly Asp
 370 375 380

Trp Asn Thr Thr Leu Ala Cys Phe Val Ala Ile Leu Ile Gly Leu Cys
 385 390 395 400

Leu Thr Leu Leu Leu Leu Ala Val Phe Lys Lys Ala Leu Pro Ala Leu
 405 410 415

Pro Ile Ser Ile Thr Phe Gly Leu Ile Phe Tyr Phe Ser Thr Asp Asn
 420 425 430

Leu Val Arg Pro Phe Met Asp Thr Leu Ala Ser His Gln Leu Tyr Ile
 435 440 445

<210> 153

<211> 272

<212> PRT

<213> Homo sapiens

<400> 153

Met Ala Ala Lys Val Phe Glu Ser Ile Gly Lys Phe Gly Leu Ala Leu
 1 5 10 15

Ala Val Ala Gly Gly Val Val Asn Ser Ala Leu Tyr Asn Val Asp Ala
 20 25 30

Gly His Arg Ala Val Ile Phe Asp Arg Phe Arg Gly Val Gln Asp Ile
 35 40 45

Protein Complexes associated with APP-processing
 Val Val Gly Ala Gly Thr His Phe Leu Ile Pro Trp Val Gln Lys Pro
 50 55 60

Ile Ile Phe Asp Cys Arg Ser Arg Pro Arg Asn Val Pro Val Ile Thr
 65 70 75 80

Gly Ser Lys Asp Leu Gln Asn Val Asn Ile Thr Leu Arg Ile Leu Phe
 85 90 95

Arg Pro Val Ala Ser Gln Leu Pro Arg Ile Phe Thr Ser Ile Gly Glu
 100 105 110

Asp Tyr Asp Glu Arg Val Leu Pro Ser Ile Thr Thr Glu Ile Leu Lys
 115 120 125

Ser Val Val Ala Arg Phe Asp Ala Gly Glu Leu Ile Thr Gln Arg Glu
 130 135 140

Leu Val Ser Arg Gln Val Ser Asp Asp Leu Thr Glu Arg Ala Ala Thr
 145 150 155 160

Phe Gly Leu Ile Leu Asp Asp Val Ser Leu Thr His Leu Thr Phe Gly
 165 170 175

Lys Glu Phe Thr Glu Ala Val Glu Ala Lys Gln Val Ala Gln Gln Glu
 180 185 190

Ala Glu Arg Ala Arg Phe Val Val Glu Lys Ala Glu Gln Gln Lys Lys
 195 200 205

Ala Ala Ile Ile Ser Ala Glu Gly Asp Ser Lys Ala Ala Glu Leu Ile
 210 215 220

Ala Asn Ser Leu Ala Thr Ala Gly Asp Gly Leu Ile Glu Leu Arg Lys
 225 230 235 240

Leu Glu Ala Ala Glu Asp Ile Ala Tyr Gln Leu Ser Arg Ser Arg Asn
 245 250 255

Ile Thr Tyr Leu Pro Ala Gly Gln Ser Val Leu Leu Gln Leu Pro Gln
 260 265 270

<210> 154

<211> 489

<212> PRT

<213> Homo sapiens

<400> 154

Protein Complexes associated with APP-processing

Met Gly Ser Gly Pro Leu Ser Leu Pro Leu Ala Leu Ser Pro Pro Arg
 1 5 10 15

Leu Leu Leu Leu Leu Leu Ser Leu Leu Pro Val Ala Arg Ala Ser
 20 25 30

Glu Ala Glu His Arg Leu Phe Glu Arg Leu Phe Glu Asp Tyr Asn Glu
 35 40 45

Ile Ile Arg Pro Val Ala Asn Val Ser Asp Pro Val Ile Ile His Phe
 50 55 60

Glu Val Ser Met Ser Gln Leu Val Lys Val Asp Glu Val Asn Gln Ile
 65 70 75 80

Met Glu Thr Asn Leu Trp Leu Lys Gln Ile Trp Asn Asp Tyr Lys Leu
 85 90 95

Lys Trp Asn Pro Ser Asp Tyr Gly Gly Ala Glu Phe Met Arg Val Pro
 100 105 110

Ala Gln Lys Ile Trp Lys Pro Asp Ile Val Leu Tyr Asn Asn Ala Val
 115 120 125

Gly Asp Phe Gln Val Asp Asp Lys Thr Lys Ala Leu Leu Lys Tyr Thr
 130 135 140

Gly Glu Val Thr Trp Ile Pro Pro Ala Ile Phe Lys Ser Ser Cys Lys
 145 150 155 160

Ile Asp Val Thr Tyr Phe Pro Phe Asp Tyr Gln Asn Cys Thr Met Lys
 165 170 175

Phe Gly Ser Trp Ser Tyr Asp Lys Ala Lys Ile Asp Leu Val Leu Ile
 180 185 190

Gly Ser Ser Met Asn Leu Lys Asp Tyr Trp Glu Ser Gly Glu Trp Ala
 195 200 205

Ile Ile Lys Ala Pro Gly Tyr Lys His Asp Ile Lys Tyr Asn Cys Cys
 210 215 220

Glu Glu Ile Tyr Pro Asp Ile Thr Tyr Ser Leu Tyr Ile Arg Arg Leu
 225 230 235 240

Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser
 245 250 255

Phe Leu Thr Val Leu Val Phe Tyr Leu Pro Ser Asp Cys Gly Glu Lys
 260 265 270

Protein Complexes associated with APP-processing

Val Thr Leu Cys Ile Ser Val Leu Leu Ser Leu Thr Val Phe Leu Leu
 275 280 285

Val Ile Thr Glu Thr Ile Pro Ser Thr Ser Leu Val Ile Pro Leu Ile
 290 295 300

Gly Glu Tyr Leu Leu Phe Thr Met Ile Phe Val Thr Leu Ser Ile Val
 305 310 315 320

Ile Thr Val Phe Val Leu Asn Val His Tyr Arg Thr Pro Thr Thr His
 325 330 335

Thr Met Pro Ser Trp Val Lys Thr Val Phe Leu Asn Leu Leu Pro Arg
 340 345 350

Val Met Phe Met Thr Arg Pro Thr Ser Asn Glu Gly Asn Ala Gln Lys
 355 360 365

Pro Arg Pro Leu Tyr Gly Ala Glu Leu Ser Asn Leu Asn Cys Phe Ser
 370 375 380

Arg Ala Glu Ser Lys Gly Cys Lys Glu Gly Tyr Pro Cys Gln Asp Gly
 385 390 395 400

Met Cys Gly Tyr Cys His His Arg Arg Ile Lys Ile Ser Asn Phe Ser
 405 410 415

Ala Asn Leu Thr Arg Ser Ser Ser Ser Glu Ser Val Asp Ala Val Leu
 420 425 430

Ser Leu Ser Ala Leu Ser Pro Glu Ile Lys Glu Ala Ile Gln Ser Val
 435 440 445

Lys Tyr Ile Ala Glu Asn Met Lys Ala Gln Asn Glu Ala Lys Glu Glu
 450 455 460

Gln Lys Ala Gln Glu Ile Gln Gln Leu Lys Arg Lys Glu Lys Ser Thr
 465 470 475 480

Glu Thr Ser Asp Gln Glu Pro Gly Leu
 485

<210> 155

<211> 359

<212> PRT

<213> Homo sapiens

<400> 155

Protein Complexes associated with APP-processing

Met Pro Ala His Leu Leu Gln Asp Asp Ile Ser Ser Ser Tyr Thr Thr
1 5 10 15

Thr Thr Thr Ile Thr Ala Pro Pro Ser Arg Val Leu Gln Asn Gly Gly
20 25 30

Asp Lys Leu Glu Thr Met Pro Leu Tyr Leu Glu Asp Asp Ile Arg Pro
35 40 45

Asp Ile Lys Asp Asp Ile Tyr Asp Pro Thr Tyr Lys Asp Lys Glu Gly
50 55 60

Pro Ser Pro Lys Val Glu Tyr Val Trp Arg Asn Ile Ile Leu Met Ser
65 70 75 80

Leu Leu His Leu Gly Ala Leu Tyr Gly Ile Thr Leu Ile Pro Thr Cys
85 90 95

Lys Phe Tyr Thr Trp Leu Trp Gly Val Phe Tyr Tyr Phe Val Ser Ala
100 105 110

Leu Gly Ile Thr Ala Gly Ala His Arg Leu Trp Ser His Arg Ser Tyr
115 120 125

Lys Ala Arg Leu Pro Leu Arg Leu Phe Leu Ile Ile Ala Asn Thr Met
130 135 140

Ala Phe Gln Asn Asp Val Tyr Glu Trp Ala Arg Asp His Arg Ala His
145 150 155 160

His Lys Phe Ser Glu Thr His Ala Asp Pro His Asn Ser Arg Arg Gly
165 170 175

Phe Phe Phe Ser His Val Gly Trp Leu Leu Val Arg Lys His Pro Ala
180 185 190

Val Lys Glu Lys Gly Ser Thr Leu Asp Leu Ser Asp Leu Glu Ala Glu
195 200 205

Lys Leu Val Met Phe Gln Arg Arg Tyr Tyr Lys Pro Gly Leu Leu Met
210 215 220

Met Cys Phe Ile Leu Pro Thr Leu Val Pro Trp Tyr Phe Trp Gly Glu
225 230 235 240

Thr Phe Gln Asn Ser Val Phe Val Ala Thr Phe Leu Arg Tyr Ala Val
245 250 255

Val Leu Asn Ala Thr Trp Leu Val Asn Ser Ala Ala His Leu Phe Gly
260 265 270

Protein Complexes associated with APP-processing

Tyr Arg Pro Tyr Asp Lys Asn Ile Ser Pro Arg Glu Asn Ile Leu Val
 275 280 285

Ser Leu Gly Ala Val Gly Glu Gly Phe His Asn Tyr His His Ser Phe
 290 295 300

Pro Tyr Asp Tyr Ser Ala Ser Glu Tyr Arg Trp His Ile Asn Phe Thr
 305 310 315 320

Thr Phe Phe Ile Asp Cys Met Ala Ala Leu Gly Leu Ala Tyr Asp Arg
 325 330 335

Lys Lys Val Ser Lys Ala Ala Ile Leu Ala Arg Ile Lys Arg Thr Gly
 340 345 350

Asp Gly Asn Tyr Lys Ser Gly
 355

<210> 156

<211> 2799

<212> PRT

<213> Homo sapiens

<400> 156

Met Thr Ser Ile His Phe Val Val His Pro Leu Pro Gly Thr Glu Asp
 1 5 10 15

Gln Leu Asn Asp Arg Leu Arg Glu Val Ser Glu Lys Leu Asn Lys Tyr
 20 25 30

Asn Leu Asn Ser His Pro Pro Leu Asn Val Leu Glu Gln Ala Thr Ile
 35 40 45

Lys Gln Cys Val Val Gly Pro Asn His Ala Ala Phe Leu Leu Glu Asp
 50 55 60

Gly Arg Val Cys Arg Ile Gly Phe Ser Val Gln Pro Asp Arg Leu Glu
 65 70 75 80

Leu Gly Lys Pro Asp Asn Asn Asp Gly Ser Lys Leu Asn Ser Asn Ser
 85 90 95

Gly Ala Gly Arg Thr Ser Arg Pro Gly Arg Thr Ser Asp Ser Pro Trp
 100 105 110

Phe Leu Ser Gly Ser Glu Thr Leu Gly Arg Leu Ala Gly Asn Thr Leu
 115 120 125

Protein Complexes associated with APP-processing

Gly Ser Arg Trp Ser Ser Gly Val Gly Gly Ser Gly Gly Gly Ser Ser
 130 135 140

Gly Arg Ser Ser Ala Gly Ala Arg Asp Ser Arg Arg Gln Thr Arg Val
 145 150 155 160

Ile Arg Thr Gly Arg Asp Arg Gly Ser Gly Leu Leu Gly Ser Gln Pro
 165 170 175

Gln Pro Val Ile Pro Ala Ser Val Ile Pro Glu Glu Leu Ile Ser Gln
 180 185 190

Ala Gln Val Val Leu Gln Gly Lys Ser Arg Ser Val Ile Ile Arg Glu
 195 200 205

Leu Gln Arg Thr Asn Leu Asp Val Asn Leu Ala Val Asn Asn Leu Leu
 210 215 220

Ser Arg Asp Asp Glu Asp Gly Asp Asp Gly Asp Asp Thr Ala Ser Glu
 225 230 235 240

Ser Tyr Leu Pro Gly Glu Asp Leu Met Ser Leu Leu Asp Ala Asp Ile
 245 250 255

His Ser Ala His Pro Ser Val Ile Ile Asp Ala Asp Ala Met Phe Ser
 260 265 270

Glu Asp Ile Ser Tyr Phe Gly Tyr Pro Ser Phe Arg Arg Ser Ser Leu
 275 280 285

Ser Arg Leu Gly Ser Ser Arg Val Leu Leu Leu Pro Leu Glu Arg Asp
 290 295 300

Ser Glu Leu Leu Arg Glu Arg Glu Ser Val Leu Arg Leu Arg Glu Arg
 305 310 315 320

Arg Trp Leu Asp Gly Ala Ser Phe Asp Asn Glu Arg Gly Ser Thr Ser
 325 330 335

Lys Glu Gly Glu Pro Asn Leu Asp Lys Lys Asn Thr Pro Val Gln Ser
 340 345 350

Pro Val Ser Leu Gly Glu Asp Leu Gln Trp Trp Pro Asp Lys Asp Gly
 355 360 365

Thr Lys Phe Ile Cys Ile Gly Ala Leu Tyr Ser Glu Leu Leu Ala Val
 370 375 380

Ser Ser Lys Gly Glu Leu Tyr Gln Trp Lys Trp Ser Glu Ser Glu Pro
 385 390 395 400

Protein Complexes associated with APP-processing

Tyr Arg Asn Ala Gln Asn Pro Ser Leu His His Pro Arg Ala Thr Phe
405 410 415

Leu Gly Leu Thr Asn Glu Lys Ile Val Leu Leu Ser Ala Asn Ser Ile
420 425 430

Arg Ala Thr Val Ala Thr Glu Asn Asn Lys Val Ala Thr Trp Val Asp
435 440 445

Glu Thr Leu Ser Ser Val Ala Ser Lys Leu Glu His Thr Ala Gln Thr
450 455 460

Tyr Ser Glu Leu Gln Gly Glu Arg Ile Val Ser Leu His Cys Cys Ala
465 470 475 480

Leu Tyr Thr Cys Ala Gln Leu Glu Asn Ser Leu Tyr Trp Trp Gly Val
485 490 495

Val Pro Phe Ser Gln Arg Lys Lys Met Leu Glu Lys Ala Arg Ala Lys
500 505 510

Asn Lys Lys Pro Lys Ser Ser Ala Gly Ile Ser Ser Met Pro Asn Ile
515 520 525

Thr Val Gly Thr Gln Val Cys Leu Arg Asn Asn Pro Leu Tyr His Ala
530 535 540

Gly Ala Val Ala Phe Ser Ile Ser Ala Gly Ile Pro Lys Val Gly Val
545 550 555 560

Leu Met Glu Ser Val Trp Asn Met Asn Asp Ser Cys Arg Phe Gln Leu
565 570 575

Arg Ser Pro Glu Ser Leu Lys Asn Met Glu Lys Ala Ser Lys Thr Thr
580 585 590

Glu Ala Lys Pro Glu Ser Lys Gln Glu Pro Val Lys Thr Glu Met Gly
595 600 605

Pro Pro Pro Ser Pro Ala Ser Thr Cys Ser Asp Ala Ser Ser Ile Ala
610 615 620

Ser Ser Ala Ser Met Pro Tyr Lys Arg Arg Arg Ser Thr Pro Ala Pro
625 630 635 640

Lys Glu Glu Glu Lys Val Asn Glu Glu Gln Trp Ser Leu Arg Glu Val
645 650 655

Val Phe Val Glu Asp Val Lys Asn Val Pro Val Gly Lys Val Leu Lys
660 665 670

Protein Complexes associated with APP-processing

Val Asp Gly Ala Tyr Val Ala Val Lys Phe Pro Gly Thr Ser Ser Asn
675 680 685

Thr Asn Cys Gln Asn Ser Ser Gly Pro Asp Ala Asp Pro Ser Ser Leu
690 695 700

Leu Gln Asp Cys Arg Leu Leu Arg Ile Asp Glu Leu Gln Val Val Lys
705 710 715 720

Thr Gly Gly Thr Pro Lys Val Pro Asp Cys Phe Gln Arg Thr Pro Lys
725 730 735

Lys Leu Cys Ile Pro Glu Lys Thr Glu Ile Leu Ala Val Asn Val Asp
740 745 750

Ser Lys Gly Val His Ala Val Leu Lys Thr Gly Asn Trp Val Arg Tyr
755 760 765

Cys Ile Phe Asp Leu Ala Thr Gly Lys Ala Glu Gln Glu Asn Asn Phe
770 775 780

Pro Thr Ser Ser Ile Ala Phe Leu Gly Gln Asn Glu Arg Asn Val Ala
785 790 795 800

Ile Phe Thr Ala Gly Gln Glu Ser Pro Ile Ile Leu Arg Asp Gly Asn
805 810 815

Gly Thr Ile Tyr Pro Met Ala Lys Asp Cys Met Gly Gly Ile Arg Asp
820 825 830

Pro Asp Trp Leu Asp Leu Pro Pro Ile Ser Ser Leu Gly Met Gly Val
835 840 845

His Ser Leu Ile Asn Leu Pro Ala Asn Ser Thr Ile Lys Lys Lys Ala
850 855 860

Ala Val Ile Ile Met Ala Val Glu Lys Gln Thr Leu Met Gln His Ile
865 870 875 880

Leu Arg Cys Asp Tyr Glu Ala Cys Arg Gln Tyr Leu Met Asn Leu Glu
885 890 895

Gln Ala Val Val Leu Glu Gln Asn Leu Gln Met Leu Gln Thr Phe Ile
900 905 910

Ser His Arg Cys Asp Gly Asn Arg Asn Ile Leu His Ala Cys Val Ser
915 920 925

Val Cys Phe Pro Thr Ser Asn Lys Glu Thr Lys Glu Glu Glu Glu Ala
930 935 940

Protein Complexes associated with APP-processing

Glu Arg Ser Glu Arg Asn Thr Phe Ala Glu Arg Leu Ser Ala Val Glu
 945 950 955 960

Ala Ile Ala Asn Ala Ile Ser Val Val Ser Ser Asn Gly Pro Gly Asn
 965 970 975

Arg Ala Gly Ser Ser Ser Ser Arg Ser Leu Arg Leu Arg Glu Met Met
 980 985 990

Arg Arg Ser Leu Arg Ala Ala Gly Leu Gly Arg His Glu Ala Gly Ala
 995 1000 1005

Ser Ser Ser Asp His Gln Asp Pro Val Ser Pro Pro Ile Ala Pro
 1010 1015 1020

Pro Ser Trp Val Pro Asp Pro Pro Ala Met Asp Pro Asp Gly Asp
 1025 1030 1035

Ile Asp Phe Ile Leu Ala Pro Ala Val Gly Ser Leu Thr Thr Ala
 1040 1045 1050

Ala Thr Gly Thr Gly Gln Gly Pro Ser Thr Ser Thr Ile Pro Gly
 1055 1060 1065

Pro Ser Thr Glu Pro Ser Val Val Glu Ser Lys Asp Arg Lys Ala
 1070 1075 1080

Asn Ala His Phe Ile Leu Lys Leu Leu Cys Asp Ser Val Val Leu
 1085 1090 1095

Gln Pro Tyr Leu Arg Glu Leu Leu Ser Ala Lys Asp Ala Arg Gly
 1100 1105 1110

Met Thr Pro Phe Met Ser Ala Val Ser Gly Arg Ala Tyr Pro Ala
 1115 1120 1125

Ala Ile Thr Ile Leu Glu Thr Ala Gln Lys Ile Ala Lys Ala Glu
 1130 1135 1140

Ile Ser Ser Ser Glu Lys Glu Glu Asp Val Phe Met Gly Met Val
 1145 1150 1155

Cys Pro Ser Gly Thr Asn Pro Asp Asp Ser Pro Leu Tyr Val Leu
 1160 1165 1170

Cys Cys Asn Asp Thr Cys Ser Phe Thr Trp Thr Gly Ala Glu His
 1175 1180 1185

Ile Asn Gln Asp Ile Phe Glu Cys Arg Thr Cys Gly Leu Leu Glu
 1190 1195 1200

protein complexes associated with APP-processing

Ser Leu Cys Cys Cys Thr Glu Cys Ala Arg Val Cys His Lys Gly
 1205 1210 1215

His Asp Cys Lys Leu Lys Arg Thr Ser Pro Thr Ala Tyr Cys Asp
 1220 1225 1230

Cys Trp Glu Lys Cys Lys Cys Lys Thr Leu Ile Ala Gly Gln Lys
 1235 1240 1245

Ser Ala Arg Leu Asp Leu Leu Tyr Arg Leu Leu Thr Ala Thr Asn
 1250 1255 1260

Leu Val Thr Leu Pro Asn Ser Arg Gly Glu His Leu Leu Leu Phe
 1265 1270 1275

Leu Val Gln Thr Val Ala Arg Gln Thr Val Glu His Cys Gln Tyr
 1280 1285 1290

Arg Pro Pro Arg Ile Arg Glu Asp Arg Asn Arg Lys Thr Ala Ser
 1295 1300 1305

Pro Glu Asp Ser Asp Met Pro Asp His Asp Leu Glu Pro Pro Arg
 1310 1315 1320

Phe Ala Gln Leu Ala Leu Glu Arg Val Leu Gln Asp Trp Asn Ala
 1325 1330 1335

Leu Lys Ser Met Ile Met Phe Gly Ser Gln Glu Asn Lys Asp Pro
 1340 1345 1350

Leu Ser Ala Ser Ser Arg Ile Gly His Leu Leu Pro Glu Glu Gln
 1355 1360 1365

Val Tyr Leu Asn Gln Gln Ser Gly Thr Ile Arg Leu Asp Cys Phe
 1370 1375 1380

Thr His Cys Leu Ile Val Lys Cys Thr Ala Asp Ile Leu Leu Leu
 1385 1390 1395

Asp Thr Leu Leu Gly Thr Leu Val Lys Glu Leu Gln Asn Lys Tyr
 1400 1405 1410

Thr Pro Gly Arg Arg Glu Glu Ala Ile Ala Val Thr Met Arg Phe
 1415 1420 1425

Leu Arg Ser Val Ala Arg Val Phe Val Ile Leu Ser Val Glu Met
 1430 1435 1440

Ala Ser Ser Lys Lys Lys Asn Asn Phe Ile Pro Gln Pro Ile Gly
 1445 1450 1455

Protein Complexes associated with APP-processing

Lys Cys Lys Arg Val Phe Gln Ala Leu Leu Pro Tyr Ala Val Glu
 1460 1465 1470

Glu Leu Cys Asn Val Ala Glu Ser Leu Ile Val Pro Val Arg Met
 1475 1480 1485

Gly Ile Ala Arg Pro Thr Ala Pro Phe Thr Leu Ala Ser Thr Ser
 1490 1495 1500

Ile Asp Ala Met Gln Gly Ser Glu Glu Leu Phe Ser Val Glu Pro
 1505 1510 1515

Leu Pro Pro Arg Pro Ser Ser Asp Gln Ser Ser Ser Ser Ser Gln
 1520 1525 1530

Ser Gln Ser Ser Tyr Ile Ile Arg Asn Pro Gln Gln Arg Arg Ile
 1535 1540 1545

Ser Gln Ser Gln Pro Val Arg Gly Arg Asp Glu Glu Gln Asp Asp
 1550 1555 1560

Ile Val Ser Ala Asp Val Glu Glu Val Glu Val Val Glu Gly Val
 1565 1570 1575

Ala Gly Glu Glu Asp His His Asp Glu Gln Glu Glu His Gly Glu
 1580 1585 1590

Glu Asn Ala Glu Ala Glu Gly Gln His Asp Glu His Asp Glu Asp
 1595 1600 1605

Gly Ser Asp Met Glu Leu Asp Leu Leu Ala Ala Ala Glu Thr Glu
 1610 1615 1620

Ser Asp Ser Glu Ser Asn His Ser Asn Gln Asp Asn Ala Ser Gly
 1625 1630 1635

Arg Arg Ser Val Val Thr Ala Ala Thr Ala Gly Ser Glu Ala Gly
 1640 1645 1650

Ala Ser Ser Val Pro Ala Phe Phe Ser Glu Asp Asp Ser Gln Ser
 1655 1660 1665

Asn Asp Ser Ser Asp Ser Asp Ser Ser Ser Ser Gln Ser Asp Asp
 1670 1675 1680

Ile Glu Gln Glu Thr Phe Met Leu Asp Glu Pro Leu Glu Arg Thr
 1685 1690 1695

Thr Asn Ser Ser His Ala Asn Gly Ala Ala Gln Ala Pro Arg Ser
 1700 1705 1710

Protein Complexes associated with APP-processing

Met Gln Trp Ala Val Arg Asn Thr Gln His Gln Arg Ala Ala Ser
 1715 1720 1725

Thr Ala Pro Ser Ser Thr Ser Thr Pro Ala Ala Ser Ser Ala Gly
 1730 1735 1740

Leu Ile Tyr Ile Asp Pro Ser Asn Leu Arg Arg Ser Gly Thr Ile
 1745 1750 1755

Ser Thr Ser Ala Ala Ala Ala Ala Ala Ala Leu Glu Ala Ser Asn
 1760 1765 1770

Ala Ser Ser Tyr Leu Thr Ser Ala Ser Ser Leu Ala Arg Ala Tyr
 1775 1780 1785

Ser Ile Val Ile Arg Gln Ile Ser Asp Leu Met Gly Leu Ile Pro
 1790 1795 1800

Lys Tyr Asn His Leu Val Tyr Ser Gln Ile Pro Ala Ala Val Lys
 1805 1810 1815

Leu Thr Tyr Gln Asp Ala Val Asn Leu Gln Asn Tyr Val Glu Glu
 1820 1825 1830

Lys Leu Ile Pro Thr Trp Asn Trp Met Val Ser Ile Met Asp Ser
 1835 1840 1845

Thr Glu Ala Gln Leu Arg Tyr Gly Ser Ala Leu Ala Ser Ala Gly
 1850 1855 1860

Asp Pro Gly His Pro Asn His Pro Leu His Ala Ser Gln Asn Ser
 1865 1870 1875

Ala Arg Arg Glu Arg Met Thr Ala Arg Glu Glu Ala Ser Leu Arg
 1880 1885 1890

Thr Leu Glu Gly Arg Arg Arg Ala Thr Leu Leu Ser Ala Arg Gln
 1895 1900 1905

Gly Met Met Ser Ala Arg Gly Asp Phe Leu Asn Tyr Ala Leu Ser
 1910 1915 1920

Leu Met Arg Ser His Asn Asp Glu His Ser Asp Val Leu Pro Val
 1925 1930 1935

Leu Asp Val Cys Ser Leu Lys His Val Ala Tyr Val Phe Gln Ala
 1940 1945 1950

Leu Ile Tyr Trp Ile Lys Ala Met Asn Gln Gln Thr Thr Leu Asp
 1955 1960 1965

Protein Complexes associated with APP-processing

Thr	Pro	Gln	Leu	Glu	Arg	Lys	Arg	Thr	Arg	Glu	Leu	Leu	Glu	Leu
	1970					1975					1980			
Gly	Ile	Asp	Asn	Glu	Asp	Ser	Glu	His	Glu	Asn	Asp	Asp	Asp	Thr
	1985					1990					1995			
Asn	Gln	Ser	Ala	Thr	Leu	Asn	Asp	Lys	Asp	Asp	Asp	Ser	Leu	Pro
	2000					2005					2010			
Ala	Glu	Thr	Gly	Gln	Asn	His	Pro	Phe	Phe	Arg	Arg	Ser	Asp	Ser
	2015					2020					2025			
Met	Thr	Phe	Leu	Gly	Cys	Ile	Pro	Pro	Asn	Pro	Phe	Glu	Val	Pro
	2030					2035					2040			
Leu	Ala	Glu	Ala	Ile	Pro	Leu	Ala	Asp	Gln	Pro	His	Leu	Leu	Gln
	2045					2050					2055			
Pro	Asn	Ala	Arg	Lys	Glu	Asp	Leu	Phe	Gly	Arg	Pro	Ser	Gln	Gly
	2060					2065					2070			
Leu	Tyr	Ser	Ser	Ser	Ala	Ser	Ser	Gly	Lys	Cys	Leu	Met	Glu	Val
	2075					2080					2085			
Thr	Val	Asp	Arg	Asn	Cys	Leu	Glu	Val	Leu	Pro	Thr	Lys	Met	Ser
	2090					2095					2100			
Tyr	Ala	Ala	Asn	Leu	Lys	Asn	Val	Met	Asn	Met	Gln	Asn	Arg	Gln
	2105					2110					2115			
Lys	Lys	Glu	Gly	Glu	Glu	Gln	Pro	Val	Leu	Pro	Glu	Glu	Thr	Glu
	2120					2125					2130			
Ser	Ser	Lys	Pro	Gly	Pro	Ser	Ala	His	Asp	Leu	Ala	Ala	Gln	Leu
	2135					2140					2145			
Lys	Ser	Ser	Leu	Leu	Ala	Glu	Ile	Gly	Leu	Thr	Glu	Ser	Glu	Gly
	2150					2155					2160			
Pro	Pro	Leu	Thr	Ser	Phe	Arg	Pro	Gln	Cys	Ser	Phe	Met	Gly	Met
	2165					2170					2175			
Val	Ile	Ser	His	Asp	Met	Leu	Leu	Gly	Arg	Trp	Arg	Leu	Ser	Leu
	2180					2185					2190			
Glu	Leu	Phe	Gly	Arg	Val	Phe	Met	Glu	Asp	Val	Gly	Ala	Glu	Pro
	2195					2200					2205			
Gly	Ser	Ile	Leu	Thr	Glu	Leu	Gly	Gly	Phe	Glu	Val	Lys	Glu	Ser
	2210					2215					2220			

Protein Complexes associated with APP-processing

Lys Phe Arg Arg Glu Met Glu Lys Leu Arg Asn Gln Gln Ser Arg
 2225 2230 2235

Asp Leu Ser Leu Glu Val Asp Arg Asp Arg Asp Leu Leu Ile Gln
 2240 2245 2250

Gln Thr Met Arg Gln Leu Asn Asn His Phe Gly Arg Arg Cys Ala
 2255 2260 2265

Thr Thr Pro Met Ala Val His Arg Val Lys Val Thr Phe Lys Asp
 2270 2275 2280

Glu Pro Gly Glu Gly Ser Gly Val Ala Arg Ser Phe Tyr Thr Ala
 2285 2290 2295

Ile Ala Gln Ala Phe Leu Ser Asn Glu Lys Leu Pro Asn Leu Glu
 2300 2305 2310

Cys Ile Gln Asn Ala Asn Lys Gly Thr His Thr Ser Leu Met Gln
 2315 2320 2325

Arg Leu Arg Asn Arg Gly Glu Arg Asp Arg Glu Arg Glu Arg Glu
 2330 2335 2340

Arg Glu Met Arg Arg Ser Ser Gly Leu Arg Ala Gly Ser Arg Arg
 2345 2350 2355

Asp Arg Asp Arg Asp Phe Arg Arg Gln Leu Ser Ile Asp Thr Arg
 2360 2365 2370

Pro Phe Arg Pro Ala Ser Glu Gly Asn Pro Ser Asp Asp Pro Glu
 2375 2380 2385

Pro Leu Pro Ala His Arg Gln Ala Leu Gly Glu Arg Leu Tyr Pro
 2390 2395 2400

Arg Val Gln Ala Met Gln Pro Ala Phe Ala Ser Lys Ile Thr Gly
 2405 2410 2415

Met Leu Leu Glu Leu Ser Pro Ala Gln Leu Leu Leu Leu Leu Ala
 2420 2425 2430

Ser Glu Asp Ser Leu Arg Ala Arg Val Asp Glu Ala Met Glu Leu
 2435 2440 2445

Ile Ile Ala His Gly Arg Glu Asn Gly Ala Asp Ser Ile Leu Asp
 2450 2455 2460

Leu Gly Leu Val Asp Ser Ser Glu Lys Val Gln Gln Glu Asn Arg
 2465 2470 2475

Protein Complexes associated with APP-processing
 Lys Arg His Gly Ser Ser Arg Ser Val Val Asp Met Asp Leu Asp
 2480 2485 2490

Asp Thr Asp Asp Gly Asp Asp Asn Ala Pro Leu Phe Tyr Gln Pro
 2495 2500 2505

Gly Lys Arg Gly Phe Tyr Thr Pro Arg Pro Gly Lys Asn Thr Glu
 2510 2515 2520

Ala Arg Leu Asn Cys Phe Arg Asn Ile Gly Arg Ile Leu Gly Leu
 2525 2530 2535

Cys Leu Leu Gln Asn Glu Leu Cys Pro Ile Thr Leu Asn Arg His
 2540 2545 2550

Val Ile Lys Val Leu Leu Gly Arg Lys Val Asn Trp His Asp Phe
 2555 2560 2565

Ala Phe Phe Asp Pro Val Met Tyr Glu Ser Leu Arg Gln Leu Ile
 2570 2575 2580

Leu Ala Ser Gln Ser Ser Asp Ala Asp Ala Val Phe Ser Ala Met
 2585 2590 2595

Asp Leu Ala Phe Ala Ile Asp Leu Cys Lys Glu Glu Gly Gly Gly
 2600 2605 2610

Gln Val Glu Leu Ile Pro Asn Gly Val Asn Ile Pro Val Thr Pro
 2615 2620 2625

Gln Asn Val Tyr Glu Tyr Val Arg Lys Tyr Ala Glu His Arg Met
 2630 2635 2640

Leu Val Val Ala Glu Gln Pro Leu His Ala Met Arg Lys Gly Leu
 2645 2650 2655

Leu Asp Val Leu Pro Lys Asn Ser Leu Glu Asp Leu Thr Ala Glu
 2660 2665 2670

Asp Phe Arg Leu Leu Val Asn Gly Cys Gly Glu Val Asn Val Gln
 2675 2680 2685

Met Leu Ile Ser Phe Thr Ser Phe Asn Asp Glu Ser Gly Glu Asn
 2690 2695 2700

Ala Glu Lys Leu Leu Gln Phe Lys Arg Trp Phe Trp Ser Ile Val
 2705 2710 2715

Glu Lys Met Ser Met Thr Glu Arg Gln Asp Leu Val Tyr Phe Trp
 2720 2725 2730

Protein Complexes associated with APP-processing

Thr Ser Ser Pro Ser Leu Pro Ala Ser Glu Glu Gly Phe Gln Pro
 2735 2740 2745

Met Pro Ser Ile Thr Ile Arg Pro Pro Asp Asp Gln His Leu Pro
 2750 2755 2760

Thr Ala Asn Thr Cys Ile Ser Arg Leu Tyr Val Pro Leu Tyr Ser
 2765 2770 2775

Ser Lys Gln Ile Leu Lys Gln Lys Leu Leu Leu Ala Ile Lys Thr
 2780 2785 2790

Lys Asn Phe Gly Phe Val
 2795

<210> 157

<211> 294

<212> PRT

<213> Homo sapiens

<400> 157

Met Ala Thr His Gly Gln Thr Cys Ala Arg Pro Met Cys Ile Pro Pro
 1 5 10 15

Ser Tyr Ala Asp Leu Gly Lys Val Ala Arg Asp Ile Phe Asn Lys Gly
 20 25 30

Phe Gly Phe Gly Leu Val Lys Leu Asp Val Lys Thr Lys Ser Cys Ser
 35 40 45

Gly Val Glu Phe Ser Thr Ser Gly Ser Ser Asn Thr Asp Thr Gly Lys
 50 55 60

Val Thr Gly Thr Leu Glu Thr Lys Tyr Lys Trp Cys Glu Tyr Gly Leu
 65 70 75 80

Thr Phe Thr Glu Lys Trp Asn Thr Asp Asn Thr Leu Gly Thr Glu Ile
 85 90 95

Ala Ile Glu Asp Gln Ile Cys Gln Gly Leu Lys Leu Thr Phe Asp Thr
 100 105 110

Thr Phe Ser Pro Asn Thr Gly Lys Lys Ser Gly Lys Ile Lys Ser Ser
 115 120 125

Tyr Lys Arg Glu Cys Ile Asn Leu Gly Cys Asp Val Asp Phe Asp Phe
 130 135 140

Protein Complexes associated with APP-processing
 Ala Gly Pro Ala Ile His Gly Ser Ala Val Phe Gly Tyr Glu Gly Trp
 145 150 155 160

Leu Ala Gly Tyr Gln Met Thr Phe Asp Ser Ala Lys Ser Lys Leu Thr
 165 170 175

Arg Asn Asn Phe Ala Val Gly Tyr Arg Thr Gly Asp Phe Gln Leu His
 180 185 190

Thr Asn Val Asn Asp Gly Thr Glu Phe Gly Gly Ser Ile Tyr Gln Lys
 195 200 205

Val Cys Glu Asp Leu Asp Thr Ser Val Asn Leu Ala Trp Thr Ser Gly
 210 215 220

Thr Asn Cys Thr Arg Phe Gly Ile Ala Ala Lys Tyr Gln Leu Asp Pro
 225 230 235 240

Thr Ala Ser Ile Ser Ala Lys Val Asn Asn Ser Ser Leu Ile Gly Val
 245 250 255

Gly Tyr Thr Gln Thr Leu Arg Pro Gly Val Lys Leu Thr Leu Ser Ala
 260 265 270

Leu Val Asp Gly Lys Ser Ile Asn Ala Gly Gly His Lys Val Gly Leu
 275 280 285

Ala Leu Glu Leu Glu Ala
 290

<210> 158

<211> 890

<212> PRT

<213> Homo sapiens

<400> 158

Met Asp Ser Asn Thr Ala Pro Leu Gly Pro Ser Cys Pro Gln Pro Pro
 1 5 10 15

Pro Ala Pro Gln Pro Gln Ala Arg Ser Arg Leu Asn Ala Thr Ala Ser
 20 25 30

Leu Glu Gln Glu Arg Ser Glu Arg Pro Arg Ala Pro Gly Pro Gln Ala
 35 40 45

Gly Pro Gly Pro Gly Val Arg Asp Ala Ala Ala Pro Ala Glu Pro Gln
 50 55 60

Protein Complexes associated with APP-processing

Ala Gln His Thr Arg Ser Arg Glu Arg Ala Asp Gly Thr Gly Pro Thr
65 70 75 80

Lys Gly Asp Met Glu Ile Pro Phe Glu Glu Val Leu Glu Arg Ala Lys
85 90 95

Ala Gly Asp Pro Lys Ala Gln Thr Glu Val Gly Lys His Tyr Leu Gln
100 105 110

Leu Ala Gly Asp Thr Asp Glu Glu Leu Asn Ser Cys Thr Ala Val Asp
115 120 125

Trp Leu Val Leu Ala Ala Lys Gln Gly Arg Arg Glu Ala Val Lys Leu
130 135 140

Leu Arg Arg Cys Leu Ala Asp Arg Arg Gly Ile Thr Ser Glu Asn Glu
145 150 155 160

Arg Glu Val Arg Gln Leu Ser Ser Glu Thr Asp Leu Glu Arg Ala Val
165 170 175

Arg Lys Ala Ala Leu Val Met Tyr Trp Lys Leu Asn Pro Lys Lys Lys
180 185 190

Lys Gln Val Ala Val Ala Glu Leu Leu Glu Asn Val Gly Gln Val Asn
195 200 205

Glu His Asp Gly Gly Ala Gln Pro Gly Pro Val Pro Lys Ser Leu Gln
210 215 220

Lys Gln Arg Arg Met Leu Glu Arg Leu Val Ser Ser Glu Ser Lys Asn
225 230 235 240

Tyr Ile Ala Leu Asp Asp Phe Val Glu Ile Thr Lys Lys Tyr Ala Lys
245 250 255

Gly Val Ile Pro Ser Ser Leu Phe Leu Gln Asp Asp Glu Asp Asp Asp
260 265 270

Glu Leu Ala Gly Lys Ser Pro Glu Asp Leu Pro Leu Arg Leu Lys Val
275 280 285

Val Lys Tyr Pro Leu His Ala Ile Met Glu Ile Lys Glu Tyr Leu Ile
290 295 300

Asp Met Ala Ser Arg Ala Gly Met His Trp Leu Ser Thr Ile Ile Pro
305 310 315 320

Thr His His Ile Asn Ala Leu Ile Phe Phe Phe Ile Ile Ser Asn Leu
325 330 335

Protein Complexes associated with APP-processing

Thr Ile Asp Phe Phe Ala Phe Phe Ile Pro Leu Val Ile Phe Tyr Leu
 340 345 350

Ser Phe Ile Ser Met Val Ile Cys Thr Leu Lys Val Phe Gln Asp Ser
 355 360 365

Lys Ala Trp Glu Asn Phe Arg Thr Leu Thr Asp Leu Leu Leu Arg Phe
 370 375 380

Glu Pro Asn Leu Asp Val Glu Gln Ala Glu Val Asn Phe Gly Trp Asn
 385 390 395 400

His Leu Glu Pro Tyr Ala His Phe Leu Leu Ser Val Phe Phe Val Ile
 405 410 415

Phe Ser Phe Pro Ile Ala Ser Lys Asp Cys Ile Pro Cys Ser Glu Leu
 420 425 430

Ala Val Ile Thr Gly Phe Phe Thr Val Thr Ser Tyr Leu Ser Leu Ser
 435 440 445

Thr His Ala Glu Pro Tyr Thr Arg Arg Ala Leu Ala Thr Glu Val Thr
 450 455 460

Ala Gly Leu Leu Ser Leu Leu Pro Ser Met Pro Leu Asn Trp Pro Tyr
 465 470 475 480

Leu Lys Val Leu Gly Gln Thr Phe Ile Thr Val Pro Val Gly His Leu
 485 490 495

Val Val Leu Asn Val Ser Val Pro Cys Leu Leu Tyr Val Tyr Leu Leu
 500 505 510

Tyr Leu Phe Phe Arg Met Ala Gln Leu Arg Asn Phe Lys Gly Thr Tyr
 515 520 525

Cys Tyr Leu Val Pro Tyr Leu Val Cys Phe Met Trp Cys Glu Leu Ser
 530 535 540

Val Val Ile Leu Leu Glu Ser Thr Gly Leu Gly Leu Leu Arg Ala Ser
 545 550 555 560

Ile Gly Tyr Phe Leu Phe Leu Phe Ala Leu Pro Ile Leu Val Ala Gly
 565 570 575

Leu Ala Leu Val Gly Val Leu Gln Phe Ala Arg Trp Phe Thr Ser Leu
 580 585 590

Glu Leu Thr Lys Ile Ala Val Thr Val Ala Val Cys Ser Val Pro Leu
 595 600 605

Protein Complexes associated with APP-processing

Leu 610 Leu Arg Trp Trp Thr Lys 615 Ala Ser Phe Ser Val Val Gly Met Val 620
 Lys 625 Ser Leu Thr Arg Ser 630 Ser Met Val Lys 635 Leu Ile Leu Val Trp Leu 640
 Thr Ala Ile Val Leu 645 Phe Cys Trp Phe Tyr 650 Val Tyr Arg Ser Glu Gly 655
 Met Lys Val Tyr 660 Asn Ser Thr Leu Thr 665 Trp Gln Gln Tyr Gly Ala Leu 670
 Cys Gly Pro 675 Arg Ala Trp Lys Glu 680 Thr Asn Met Ala Arg Thr Gln Ile 685
 Leu 690 Cys Ser His Leu Glu Gly 695 His Arg Val Thr Trp Thr Gly Arg Phe 700
 Lys 705 Tyr Val Arg Val Thr 710 Asp Ile Asp Asn Ser 715 Ala Glu Ser Ala Ile 720
 Asn Met Leu Pro Phe 725 Phe Ile Gly Asp Trp 730 Met Arg Cys Leu Tyr Gly 735
 Glu Ala Tyr Pro 740 Ala Cys Ser Pro Gly 745 Asn Thr Ser Thr Ala Glu Glu 750
 Glu Leu Cys 755 Arg Leu Lys Leu 760 Ala Lys His Pro Cys 765 His Ile Lys 770
 Lys 770 Phe Asp Arg Tyr Lys Phe 775 Glu Ile Thr Val Gly 780 Met Pro Phe Ser 785
 Ser Gly Ala Asp Gly 790 Ser Arg Ser Arg Glu Glu 795 Asp Asp Val Thr Lys 800
 Asp Ile Val Leu 805 Arg Ala Ser Ser Glu Phe 810 Lys Ser Val Leu Leu Ser 815
 Leu Arg Gln Gly 820 Ser Leu Ile Glu Phe 825 Ser Thr Ile Leu Glu Gly Arg 830
 Leu Gly Ser 835 Lys Trp Pro Val Phe 840 Glu Leu Lys Ala Ile 845 Ser Cys Leu 850
 Asn Cys Met Ala Gln Leu 855 Ser Pro Thr Arg Arg His 860 Val Lys Ile Glu 865
 His 865 Asp Trp Arg Ser Thr 870 Val His Gly Ala Val 875 Lys Phe Ala Phe Asp 880

Protein Complexes associated with APP-processing
 Phe Phe Phe Phe Pro Phe Leu Ser Ala Ala
 885 890

<210> 159

<211> 226

<212> PRT

<213> Homo sapiens

<400> 159

Met Ala Ala Ala Ala Val Gln Gly Gly Arg Ser Gly Gly Ser Gly Gly
 1 5 10 15

Cys Ser Gly Ala Gly Gly Ala Ser Asn Cys Gly Thr Gly Ser Gly Arg
 20 25 30

Ser Gly Leu Leu Asp Lys Trp Lys Ile Asp Asp Lys Pro Val Lys Ile
 35 40 45

Asp Lys Trp Asp Gly Ser Ala Val Lys Asn Ser Leu Asp Asp Ser Ala
 50 55 60

Lys Lys Val Leu Leu Glu Lys Tyr Lys Tyr Val Glu Asn Phe Gly Leu
 65 70 75 80

Ile Asp Gly Arg Leu Thr Ile Cys Thr Ile Ser Cys Phe Phe Ala Ile
 85 90 95

Val Ala Leu Ile Trp Asp Tyr Met His Pro Phe Pro Glu Ser Lys Pro
 100 105 110

Val Leu Ala Leu Cys Val Ile Ser Tyr Phe Val Met Met Gly Ile Leu
 115 120 125

Thr Ile Tyr Thr Ser Tyr Lys Glu Lys Ser Ile Phe Leu Val Ala His
 130 135 140

Arg Lys Asp Pro Thr Gly Met Asp Pro Asp Asp Ile Trp Gln Leu Ser
 145 150 155 160

Ser Ser Leu Lys Arg Phe Asp Asp Lys Tyr Thr Leu Lys Leu Thr Phe
 165 170 175

Ile Ser Gly Arg Thr Lys Gln Gln Arg Glu Ala Glu Phe Thr Lys Ser
 180 185 190

Ile Ala Lys Phe Phe Asp His Ser Gly Thr Leu Val Met Asp Ala Tyr
 195 200 205

Protein Complexes associated with APP-processing
 Glu Pro Glu Ile Ser Arg Leu His Asp Ser Leu Ala Ile Glu Arg Lys
 210 215 220

Ile Lys
 225

<210> 160

<211> 1704

<212> PRT

<213> Homo sapiens

<400> 160

Met Ala Val Leu Arg Gln Leu Ala Leu Leu Leu Trp Lys Asn Tyr Thr
 1 5 10 15

Leu Gln Lys Arg Lys Val Leu Val Thr Val Leu Glu Leu Phe Leu Pro
 20 25 30

Leu Leu Phe Pro Gly Ile Leu Ile Trp Leu Arg Leu Lys Ile Gln Ser
 35 40 45

Glu Asn Val Pro Asn Ala Thr Ile Tyr Pro Gly Gln Ser Ile Gln Glu
 50 55 60

Leu Pro Leu Phe Phe Thr Phe Pro Pro Pro Gly Asp Thr Trp Glu Leu
 65 70 75 80

Ala Tyr Ile Pro Ser His Ser Asp Ala Ala Lys Thr Val Thr Glu Thr
 85 90 95

Val Arg Arg Ala Leu Val Ile Asn Met Arg Val Arg Gly Phe Pro Ser
 100 105 110

Glu Lys Asp Phe Glu Asp Tyr Ile Arg Tyr Asp Asn Cys Ser Ser Ser
 115 120 125

Val Leu Ala Ala Val Val Phe Glu His Pro Phe Asn His Ser Lys Glu
 130 135 140

Pro Leu Pro Leu Ala Val Lys Tyr His Leu Arg Phe Ser Tyr Thr Arg
 145 150 155 160

Arg Asn Tyr Met Trp Thr Gln Thr Gly Ser Phe Phe Leu Lys Glu Thr
 165 170 175

Glu Gly Trp His Thr Thr Ser Leu Phe Pro Leu Phe Pro Asn Pro Gly
 180 185 190

Protein Complexes associated with APP-processing

Pro Arg Glu Leu Thr Ser Pro Asp Gly Gly Glu Pro Gly Tyr Ile Arg
 195 200 205

Glu Gly Phe Leu Ala Val Gln His Ala Val Asp Arg Ala Ile Met Glu
 210 215 220

Tyr His Ala Asp Ala Ala Thr Arg Gln Leu Phe Gln Arg Leu Thr Val
 225 230 235 240

Thr Ile Lys Arg Phe Pro Tyr Pro Pro Phe Ile Ala Asp Pro Phe Leu
 245 250 255

Val Ala Ile Gln Tyr Gln Leu Pro Leu Leu Leu Leu Leu Ser Phe Thr
 260 265 270

Tyr Thr Ala Leu Thr Ile Ala Arg Ala Val Val Gln Glu Lys Glu Arg
 275 280 285

Arg Leu Lys Glu Tyr Met Arg Met Met Gly Leu Ser Ser Trp Leu His
 290 295 300

Trp Ser Ala Trp Phe Leu Leu Phe Phe Leu Phe Leu Leu Ile Ala Ala
 305 310 315 320

Ser Phe Met Thr Leu Leu Phe Cys Val Lys Val Lys Pro Asn Val Ala
 325 330 335

Val Leu Ser Arg Ser Asp Pro Ser Leu Val Leu Ala Phe Leu Leu Cys
 340 345 350

Phe Ala Ile Ser Thr Ile Ser Phe Ser Phe Met Val Ser Thr Phe Phe
 355 360 365

Ser Lys Ala Asn Met Ala Ala Ala Phe Gly Gly Phe Leu Tyr Phe Phe
 370 375 380

Thr Tyr Ile Pro Tyr Phe Phe Val Ala Pro Arg Tyr Asn Trp Met Thr
 385 390 395 400

Leu Ser Gln Lys Leu Cys Ser Cys Leu Leu Ser Asn Val Ala Met Ala
 405 410 415

Met Gly Ala Gln Leu Ile Gly Lys Phe Glu Ala Lys Gly Met Gly Ile
 420 425 430

Gln Trp Arg Asp Leu Leu Ser Pro Val Asn Val Asp Asp Asp Phe Cys
 435 440 445

Phe Gly Gln Val Leu Gly Met Leu Leu Leu Asp Ser Val Leu Tyr Gly
 450 455 460

Protein Complexes associated with APP-processing

Leu Val Thr Trp Tyr Met Glu Ala Val Phe Pro Gly Gln Phe Gly Val
 465 470 475 480

Pro Gln Pro Trp Tyr Phe Phe Ile Met Pro Ser Tyr Trp Cys Gly Lys
 485 490 495

Pro Arg Ala Val Ala Gly Lys Glu Glu Glu Asp Ser Asp Pro Glu Lys
 500 505 510

Ala Leu Arg Asn Glu Tyr Phe Glu Ala Glu Pro Glu Asp Leu Val Ala
 515 520 525

Gly Ile Lys Ile Lys His Leu Ser Lys Val Phe Arg Val Gly Asn Lys
 530 535 540

Asp Arg Ala Ala Val Arg Asp Leu Asn Leu Asn Leu Tyr Glu Gly Gln
 545 550 555 560

Ile Thr Val Leu Leu Gly His Asn Gly Ala Gly Lys Thr Thr Thr Leu
 565 570 575

Ser Met Leu Thr Gly Leu Phe Pro Pro Thr Ser Gly Arg Ala Tyr Ile
 580 585 590

Ser Gly Tyr Glu Ile Ser Gln Asp Met Val Gln Ile Arg Lys Ser Leu
 595 600 605

Gly Leu Cys Pro Gln His Asp Ile Leu Phe Asp Asn Leu Thr Val Ala
 610 615 620

Glu His Leu Tyr Phe Tyr Ala Gln Leu Lys Gly Leu Ser Arg Gln Lys
 625 630 635 640

Cys Pro Glu Glu Val Lys Gln Met Leu His Ile Ile Gly Leu Glu Asp
 645 650 655

Lys Trp Asn Ser Arg Ser Arg Phe Leu Ser Gly Gly Met Arg Arg Lys
 660 665 670

Leu Ser Ile Gly Ile Ala Leu Ile Ala Gly Ser Lys Val Leu Ile Leu
 675 680 685

Asp Glu Pro Thr Ser Gly Met Asp Ala Ile Ser Arg Arg Ala Ile Trp
 690 695 700

Asp Leu Leu Gln Arg Gln Lys Ser Asp Arg Thr Ile Val Leu Thr Thr
 705 710 715 720

His Phe Met Asp Glu Ala Asp Leu Leu Gly Asp Arg Ile Ala Ile Met
 725 730 735

Protein Complexes associated with APP-processing
 Ala Lys Gly Glu Leu Gln Cys Cys Gly Ser Ser Leu Phe Leu Lys Gln
 740 745 750

Lys Tyr Gly Ala Gly Tyr His Met Thr Leu Val Lys Glu Pro His Cys
 755 760 765

Asn Pro Glu Asp Ile Ser Gln Leu Val His His His Val Pro Asn Ala
 770 775 780

Thr Leu Glu Ser Ser Ala Gly Ala Glu Leu Ser Phe Ile Leu Pro Arg
 785 790 795 800

Glu Ser Thr His Arg Phe Glu Gly Leu Phe Ala Lys Leu Glu Lys Lys
 805 810 815

Gln Lys Glu Leu Gly Ile Ala Ser Phe Gly Ala Ser Ile Thr Thr Met
 820 825 830

Glu Glu Val Phe Leu Arg Val Gly Lys Leu Val Asp Ser Ser Met Asp
 835 840 845

Ile Gln Ala Ile Gln Leu Pro Ala Leu Gln Tyr Gln His Glu Arg Arg
 850 855 860

Ala Ser Asp Trp Ala Val Asp Ser Asn Leu Cys Gly Ala Met Asp Pro
 865 870 875 880

Ser Asp Gly Ile Gly Ala Leu Ile Glu Glu Glu Arg Thr Ala Val Lys
 885 890 895

Leu Asn Thr Gly Leu Ala Leu His Cys Gln Gln Phe Trp Ala Met Phe
 900 905 910

Leu Lys Lys Ala Ala Tyr Ser Trp Arg Glu Trp Lys Met Val Ala Ala
 915 920 925

Gln Val Leu Val Pro Leu Thr Cys Val Thr Leu Ala Leu Leu Ala Ile
 930 935 940

Asn Tyr Ser Ser Glu Leu Phe Asp Asp Pro Met Leu Arg Leu Thr Leu
 945 950 955 960

Gly Glu Tyr Gly Arg Thr Val Val Pro Phe Ser Val Pro Gly Thr Ser
 965 970 975

Gln Leu Gly Gln Gln Leu Ser Glu His Leu Lys Asp Ala Leu Gln Ala
 980 985 990

Glu Gly Gln Glu Pro Arg Glu Val Leu Gly Asp Leu Glu Glu Phe Leu
 995 1000 1005

Protein Complexes associated with APP-processing

Ile	Phe	Arg	Ala	Ser	Val	Glu	Gly	Gly	Gly	Phe	Asn	Glu	Arg	Cys
	1010					1015					1020			
Leu	Val	Ala	Ala	Ser	Phe	Arg	Asp	Val	Gly	Glu	Arg	Thr	Val	Val
	1025					1030					1035			
Asn	Ala	Leu	Phe	Asn	Asn	Gln	Ala	Tyr	His	Ser	Pro	Ala	Thr	Ala
	1040					1045					1050			
Leu	Ala	Val	Val	Asp	Asn	Leu	Leu	Phe	Lys	Leu	Leu	Cys	Gly	Pro
	1055					1060					1065			
His	Ala	Ser	Ile	Val	Val	Ser	Asn	Phe	Pro	Gln	Pro	Arg	Ser	Ala
	1070					1075					1080			
Leu	Gln	Ala	Ala	Lys	Asp	Gln	Phe	Asn	Glu	Gly	Arg	Lys	Gly	Phe
	1085					1090					1095			
Asp	Ile	Ala	Leu	Asn	Leu	Leu	Phe	Ala	Met	Ala	Phe	Leu	Ala	Ser
	1100					1105					1110			
Thr	Phe	Ser	Ile	Leu	Ala	Val	Ser	Glu	Arg	Ala	Val	Gln	Ala	Lys
	1115					1120					1125			
His	Val	Gln	Phe	Val	Ser	Gly	Val	His	Val	Ala	Ser	Phe	Trp	Leu
	1130					1135					1140			
Ser	Ala	Leu	Leu	Trp	Asp	Leu	Ile	Ser	Phe	Leu	Ile	Pro	Ser	Leu
	1145					1150					1155			
Leu	Leu	Leu	Val	Val	Phe	Lys	Ala	Phe	Asp	Val	Arg	Ala	Phe	Thr
	1160					1165					1170			
Arg	Asp	Gly	His	Met	Ala	Asp	Thr	Leu	Leu	Leu	Leu	Leu	Leu	Tyr
	1175					1180					1185			
Gly	Trp	Ala	Ile	Ile	Pro	Leu	Met	Tyr	Leu	Met	Asn	Phe	Phe	Phe
	1190					1195					1200			
Leu	Gly	Ala	Ala	Thr	Ala	Tyr	Thr	Arg	Leu	Thr	Ile	Phe	Asn	Ile
	1205					1210					1215			
Leu	Ser	Gly	Ile	Ala	Thr	Phe	Leu	Met	Val	Thr	Ile	Met	Arg	Ile
	1220					1225					1230			
Pro	Ala	Val	Lys	Leu	Glu	Glu	Leu	Ser	Lys	Thr	Leu	Asp	His	Val
	1235					1240					1245			
Phe	Leu	Val	Leu	Pro	Asn	His	Cys	Leu	Gly	Met	Ala	Val	Ser	Ser
	1250					1255					1260			

Protein Complexes associated with APP-processing

Phe	Tyr	Glu	Asn	Tyr	Glu	Thr	Arg	Arg	Tyr	Cys	Thr	Ser	Ser	Glu
1265						1270					1275			
Val	Ala	Ala	His	Tyr	Cys	Lys	Lys	Tyr	Asn	Ile	Gln	Tyr	Gln	Glu
1280						1285					1290			
Asn	Phe	Tyr	Ala	Trp	Ser	Ala	Pro	Gly	Val	Gly	Arg	Phe	Val	Ala
1295						1300					1305			
Ser	Met	Ala	Ala	Ser	Gly	Cys	Ala	Tyr	Leu	Ile	Leu	Leu	Phe	Leu
1310						1315					1320			
Ile	Glu	Thr	Asn	Leu	Leu	Gln	Arg	Leu	Arg	Gly	Ile	Leu	Cys	Ala
1325						1330					1335			
Leu	Arg	Arg	Arg	Arg	Thr	Leu	Thr	Glu	Leu	Tyr	Thr	Arg	Met	Pro
1340						1345					1350			
Val	Leu	Pro	Glu	Asp	Gln	Asp	Val	Ala	Asp	Glu	Arg	Thr	Arg	Ile
1355						1360					1365			
Leu	Ala	Pro	Ser	Pro	Asp	Ser	Leu	Leu	His	Thr	Pro	Leu	Ile	Ile
1370						1375					1380			
Lys	Glu	Leu	Ser	Lys	Val	Tyr	Glu	Gln	Arg	Val	Pro	Leu	Leu	Ala
1385						1390					1395			
Val	Asp	Arg	Leu	Ser	Leu	Ala	Val	Gln	Lys	Gly	Glu	Cys	Phe	Gly
1400						1405					1410			
Leu	Leu	Gly	Phe	Asn	Gly	Ala	Gly	Lys	Thr	Thr	Thr	Phe	Lys	Met
1415						1420					1425			
Leu	Thr	Gly	Glu	Glu	Ser	Leu	Thr	Ser	Gly	Asp	Ala	Phe	Val	Gly
1430						1435					1440			
Gly	His	Arg	Ile	Ser	Ser	Asp	Val	Gly	Lys	Val	Arg	Gln	Arg	Ile
1445						1450					1455			
Gly	Tyr	Cys	Pro	Gln	Phe	Asp	Ala	Leu	Leu	Asp	His	Met	Thr	Gly
1460						1465					1470			
Arg	Glu	Met	Leu	Val	Met	Tyr	Ala	Arg	Leu	Arg	Gly	Ile	Pro	Glu
1475						1480					1485			
Arg	His	Ile	Gly	Ala	Cys	Val	Glu	Asn	Thr	Leu	Arg	Gly	Leu	Leu
1490						1495					1500			
Leu	Glu	Pro	His	Ala	Asn	Lys	Leu	Val	Arg	Thr	Tyr	Ser	Gly	Gly
1505						1510					1515			

Protein Complexes associated with APP-processing
 Asn Lys Arg Lys Leu Ser Thr Gly Ile Ala Leu Ile Gly Glu Pro
 1520 1525 1530

Ala Val Ile Phe Leu Asp Glu Pro Ser Thr Gly Met Asp Pro Val
 1535 1540 1545

Ala Arg Arg Leu Leu Trp Asp Thr Val Ala Arg Ala Arg Glu Ser
 1550 1555 1560

Gly Lys Ala Ile Ile Ile Thr Ser His Ser Met Glu Glu Cys Glu
 1565 1570 1575

Ala Leu Cys Thr Arg Leu Ala Ile Met Val Gln Gly Gln Phe Lys
 1580 1585 1590

Cys Leu Gly Ser Pro Gln His Leu Lys Ser Lys Phe Gly Ser Gly
 1595 1600 1605

Tyr Ser Leu Arg Ala Lys Val Gln Ser Glu Gly Gln Gln Glu Ala
 1610 1615 1620

Leu Glu Glu Phe Lys Ala Phe Val Asp Leu Thr Phe Pro Gly Ser
 1625 1630 1635

Val Leu Glu Asp Glu His Gln Gly Met Val His Tyr His Leu Pro
 1640 1645 1650

Gly Arg Asp Leu Ser Trp Ala Lys Val Phe Gly Ile Leu Glu Lys
 1655 1660 1665

Ala Lys Glu Lys Tyr Gly Val Asp Asp Tyr Ser Val Ser Gln Ile
 1670 1675 1680

Ser Leu Glu Gln Val Phe Leu Ser Phe Ala His Leu Gln Pro Pro
 1685 1690 1695

Thr Ala Glu Glu Gly Arg
 1700

<210> 161

<211> 501

<212> PRT

<213> Homo sapiens

<400> 161

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
 1 5 10 15

Protein Complexes associated with APP-processing

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205

Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285

Protein Complexes associated with APP-processing
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380

Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430

Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445

Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460

Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
 465 470 475 480

Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
 485 490 495

Ile Ser Leu Leu Lys
 500

<210> 162

<211> 501

<212> PRT

<213> Homo sapiens

<400> 162

Protein Complexes associated with APP-processing

Met Ala Gln Ala Leu Pro Trp Leu Leu Trp Met Gly Ala Gly Val
 1 5 10 15
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270

Protein Complexes associated with APP-processing

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285

Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380

Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430

Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445

Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460

Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
 465 470 475 480

Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
 485 490 495

Ile Ser Leu Leu Lys
 500

<210> 163

<211> 455

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 163

Met Ser Phe Leu Ile Asp Ser Ser Ile Met Ile Thr Ser Gln Ile Leu
1 5 10 15

Phe Phe Gly Phe Gly Trp Leu Phe Phe Met Arg Gln Leu Phe Lys Asp
20 25 30

Tyr Glu Ile Arg Gln Tyr Val Val Gln Val Ile Phe Ser Val Thr Phe
35 40 45

Ala Phe Ser Cys Thr Met Phe Glu Leu Ile Ile Phe Glu Ile Leu Gly
50 55 60

Val Leu Asn Ser Ser Ser Arg Tyr Phe His Trp Lys Met Asn Leu Cys
65 70 75 80

Val Ile Leu Leu Ile Leu Val Phe Met Val Pro Phe Tyr Ile Gly Tyr
85 90 95

Phe Ile Val Ser Asn Ile Arg Leu Leu His Lys Gln Arg Leu Leu Phe
100 105 110

Ser Cys Leu Leu Trp Leu Thr Phe Met Tyr Phe Phe Trp Lys Leu Gly
115 120 125

Asp Pro Phe Pro Ile Leu Ser Pro Lys His Gly Ile Leu Ser Ile Glu
130 135 140

Gln Leu Ile Ser Arg Val Gly Val Ile Gly Val Thr Leu Met Ala Leu
145 150 155 160

Leu Ser Gly Phe Gly Ala Val Asn Cys Pro Tyr Thr Tyr Met Ser Tyr
165 170 175

Phe Leu Arg Asn Val Thr Asp Thr Asp Ile Leu Ala Leu Glu Arg Arg
180 185 190

Leu Leu Gln Thr Met Asp Met Ile Ile Ser Lys Lys Lys Arg Met Ala
195 200 205

Met Ala Arg Arg Thr Met Phe Gln Lys Gly Glu Val His Asn Lys Pro
210 215 220

Ser Gly Phe Trp Gly Met Ile Lys Ser Val Thr Thr Ser Ala Ser Gly
225 230 235 240

Ser Glu Asn Leu Thr Leu Ile Gln Gln Glu Val Asp Ala Leu Glu Glu
245 250 255

Protein Complexes associated with APP-processing
 Leu Ser Arg Gln Leu Phe Leu Glu Thr Ala Asp Leu Tyr Ala Thr Lys
 260 265 270

Glu Arg Ile Glu Tyr Ser Lys Thr Phe Lys Gly Lys Tyr Phe Asn Phe
 275 280 285

Leu Gly Tyr Phe Phe Ser Ile Tyr Cys Val Trp Lys Ile Phe Met Ala
 290 295 300

Thr Ile Asn Ile Val Phe Asp Arg Val Gly Lys Thr Asp Pro Val Thr
 305 310 315 320

Arg Gly Ile Glu Ile Thr Val Asn Tyr Leu Gly Ile Gln Phe Asp Val
 325 330 335

Lys Phe Trp Ser Gln His Ile Ser Phe Ile Leu Val Gly Ile Ile Ile
 340 345 350

Val Thr Ser Ile Arg Gly Leu Leu Ile Thr Leu Thr Lys Phe Phe Tyr
 355 360 365

Ala Ile Ser Ser Ser Lys Ser Ser Asn Val Ile Val Leu Leu Leu Ala
 370 375 380

Gln Ile Met Gly Met Tyr Phe Val Ser Ser Val Leu Leu Ile Arg Met
 385 390 395 400

Ser Met Pro Leu Glu Tyr Arg Thr Ile Ile Thr Glu Val Leu Gly Glu
 405 410 415

Leu Gln Phe Asn Phe Tyr His Arg Trp Phe Asp Val Ile Phe Leu Val
 420 425 430

Ser Ala Leu Ser Ser Ile Leu Phe Leu Tyr Leu Ala His Lys Gln Ala
 435 440 445

Pro Glu Lys Gln Met Ala Pro
 450 455

<210> 164

<211> 215

<212> PRT

<213> Homo sapiens

<400> 164

Met Ser Ser Ser Glu Glu Val Ser Trp Ile Ser Trp Phe Cys Gly Leu
 1 5 10 15

Protein Complexes associated with APP-processing

Arg Gly Asn Glu Phe Phe Cys Glu Val Asp Glu Asp Tyr Ile Gln Asp
 20 25 30

Lys Phe Asn Leu Thr Gly Leu Asn Glu Gln Val Pro His Tyr Arg Gln
 35 40 45

Ala Leu Asp Met Ile Leu Asp Leu Glu Pro Asp Glu Glu Leu Glu Asp
 50 55 60

Asn Pro Asn Gln Ser Asp Leu Ile Glu Gln Ala Ala Glu Met Leu Tyr
 65 70 75 80

Gly Leu Ile His Ala Arg Tyr Ile Leu Thr Asn Arg Gly Ile Ala Gln
 85 90 95

Met Leu Glu Lys Tyr Gln Gln Gly Asp Phe Gly Tyr Cys Pro Arg Val
 100 105 110

Tyr Cys Glu Asn Gln Pro Met Leu Pro Ile Gly Leu Ser Asp Ile Pro
 115 120 125

Gly Glu Ala Met Val Lys Leu Tyr Cys Pro Lys Cys Met Asp Val Tyr
 130 135 140

Thr Pro Lys Ser Ser Arg His His His Thr Asp Gly Ala Tyr Phe Gly
 145 150 155 160

Thr Gly Phe Pro His Met Leu Phe Met Val His Pro Glu Tyr Arg Pro
 165 170 175

Lys Arg Pro Ala Asn Gln Phe Val Pro Arg Leu Tyr Gly Phe Lys Ile
 180 185 190

His Pro Met Ala Tyr Gln Leu Gln Leu Gln Ala Ala Ser Asn Phe Lys
 195 200 205

Ser Pro Val Lys Thr Ile Arg
 210 215

<210> 165

<211> 339

<212> PRT

<213> Homo sapiens

<400> 165

Met Trp Gln Leu Trp Ala Ser Leu Cys Cys Leu Leu Val Leu Ala Asn
 1 5 10 15

Protein Complexes associated with APP-processing

Ala Arg Ser Arg Pro Ser Phe His Pro Val Ser Asp Glu Leu Val Asn
 20 25 30

Tyr Val Asn Lys Arg Asn Thr Thr Trp Gln Ala Gly His Asn Phe Tyr
 35 40 45

Asn Val Asp Met Ser Tyr Leu Lys Arg Leu Cys Gly Thr Phe Leu Gly
 50 55 60

Gly Pro Lys Pro Pro Gln Arg Val Met Phe Thr Glu Asp Leu Lys Leu
 65 70 75 80

Pro Ala Ser Phe Asp Ala Arg Glu Gln Trp Pro Gln Cys Pro Thr Ile
 85 90 95

Lys Glu Ile Arg Asp Gln Gly Ser Cys Gly Ser Cys Trp Ala Phe Gly
 100 105 110

Ala Val Glu Ala Ile Ser Asp Arg Ile Cys Ile His Thr Asn Ala His
 115 120 125

Val Ser Val Glu Val Ser Ala Glu Asp Leu Leu Thr Cys Cys Gly Ser
 130 135 140

Met Cys Gly Asp Gly Cys Asn Gly Gly Tyr Pro Ala Glu Ala Trp Asn
 145 150 155 160

Phe Trp Thr Arg Lys Gly Leu Val Ser Gly Gly Leu Tyr Glu Ser His
 165 170 175

Val Gly Cys Arg Pro Tyr Ser Ile Pro Pro Cys Glu His His Val Asn
 180 185 190

Gly Ser Arg Pro Pro Cys Thr Gly Glu Gly Asp Thr Pro Lys Cys Ser
 195 200 205

Lys Ile Cys Glu Pro Gly Tyr Ser Pro Thr Tyr Lys Gln Asp Lys His
 210 215 220

Tyr Gly Tyr Asn Ser Tyr Ser Val Ser Asn Ser Glu Lys Asp Ile Met
 225 230 235 240

Ala Glu Ile Tyr Lys Asn Gly Pro Val Glu Gly Ala Phe Ser Val Tyr
 245 250 255

Ser Asp Phe Leu Leu Tyr Lys Ser Gly Val Tyr Gln His Val Thr Gly
 260 265 270

Glu Met Met Gly Gly His Ala Ile Arg Ile Leu Gly Trp Gly Val Glu
 275 280 285

Protein Complexes associated with APP-processing

Asn Gly Thr Pro Tyr Trp Leu Val Ala Asn Ser Trp Asn Thr Asp Trp
 290 295 300

Gly Asp Asn Gly Phe Phe Lys Ile Leu Arg Gly Gln Asp His Cys Gly
 305 310 315 320

Ile Glu Ser Glu Val Val Ala Gly Ile Pro Arg Thr Asp Gln Tyr Trp
 325 330 335

Glu Lys Ile

<210> 166

<211> 444

<212> PRT

<213> Homo sapiens

<400> 166

Met Gly Lys Gly Gly Asn Gln Gly Glu Gly Ala Ala Glu Arg Glu Val
 1 5 10 15

Ser Val Pro Thr Phe Ser Trp Glu Glu Ile Gln Lys His Asn Leu Arg
 20 25 30

Thr Asp Arg Trp Leu Val Ile Asp Arg Lys Val Tyr Asn Ile Thr Lys
 35 40 45

Trp Ser Ile Gln His Pro Gly Gly Gln Arg Val Ile Gly His Tyr Ala
 50 55 60

Gly Glu Asp Ala Thr Asp Ala Phe Arg Ala Phe His Pro Asp Leu Glu
 65 70 75 80

Phe Val Gly Lys Phe Leu Lys Pro Leu Leu Ile Gly Glu Leu Ala Pro
 85 90 95

Glu Glu Pro Ser Gln Asp His Gly Lys Asn Ser Lys Ile Thr Glu Asp
 100 105 110

Phe Arg Ala Leu Arg Lys Thr Ala Glu Asp Met Asn Leu Phe Lys Thr
 115 120 125

Asn His Val Phe Phe Leu Leu Leu Ala His Ile Ile Ala Leu Glu
 130 135 140

Ser Ile Ala Trp Phe Thr Val Phe Tyr Phe Gly Asn Gly Trp Ile Pro
 145 150 155 160

Protein Complexes associated with APP-processing

Thr Leu Ile Thr Ala Phe Val Leu Ala Thr Ser Gln Ala Gln Ala Gly
 165 170 175

Trp Leu Gln His Asp Tyr Gly His Leu Ser Val Tyr Arg Lys Pro Lys
 180 185 190

Trp Asn His Leu Val His Lys Phe Val Ile Gly His Leu Lys Gly Ala
 195 200 205

Ser Ala Asn Trp Trp Asn His Arg His Phe Gln His His Ala Lys Pro
 210 215 220

Asn Ile Phe His Lys Asp Pro Asp Val Asn Met Leu His Val Phe Val
 225 230 235 240

Leu Gly Glu Trp Gln Pro Ile Glu Tyr Gly Lys Lys Lys Leu Lys Tyr
 245 250 255

Leu Pro Tyr Asn His Gln His Glu Tyr Phe Phe Leu Ile Gly Pro Pro
 260 265 270

Leu Leu Ile Pro Met Tyr Phe Gln Tyr Gln Ile Ile Met Thr Met Ile
 275 280 285

Val His Lys Asn Trp Val Asp Leu Ala Trp Ala Val Ser Tyr Tyr Ile
 290 295 300

Arg Phe Phe Ile Thr Tyr Ile Pro Phe Tyr Gly Ile Leu Gly Ala Leu
 305 310 315 320

Leu Phe Leu Asn Phe Ile Arg Phe Leu Glu Ser His Trp Phe Val Trp
 325 330 335

Val Thr Gln Met Asn His Ile Val Met Glu Ile Asp Gln Glu Ala Tyr
 340 345 350

Arg Asp Trp Phe Ser Ser Gln Leu Thr Ala Thr Cys Asn Val Glu Gln
 355 360 365

Ser Phe Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu
 370 375 380

His His Leu Phe Pro Thr Met Pro Arg His Asn Leu His Lys Ile Ala
 385 390 395 400

Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Glu
 405 410 415

Lys Pro Leu Leu Arg Ala Leu Leu Asp Ile Ile Arg Ser Leu Lys Lys
 420 425 430

Protein Complexes associated with APP-processing

Ser Gly Lys Leu Trp Leu Asp Ala Tyr Leu His Lys
 435 440

<210> 167

<211> 236

<212> PRT

<213> Homo sapiens

<400> 167

Met Ala Ser Leu Asp Arg Val Lys Val Leu Val Leu Gly Asp Ser Gly
 1 5 10 15

Val Gly Lys Ser Ser Leu Val His Leu Leu Cys Gln Asn Gln Val Leu
 20 25 30

Gly Asn Pro Ser Trp Thr Val Gly Cys Ser Val Asp Val Arg Val His
 35 40 45

Asp Tyr Lys Glu Gly Thr Pro Glu Glu Lys Thr Cys Tyr Ile Glu Leu
 50 55 60

Trp Asp Val Gly Gly Ser Val Gly Ser Ala Ser Ser Val Lys Ser Thr
 65 70 75 80

Arg Ala Val Phe Tyr Asn Ser Val Asn Gly Ile Ile Phe Val His Asp
 85 90 95

Leu Thr Asn Lys Lys Ser Ser Gln Asn Leu Arg Arg Trp Ser Leu Glu
 100 105 110

Ala Leu Asn Arg Asp Leu Val Pro Thr Gly Val Leu Val Thr Asn Gly
 115 120 125

Asp Tyr Asp Gln Glu Gln Phe Ala Asp Asn Gln Ile Pro Leu Leu Val
 130 135 140

Ile Gly Thr Lys Leu Asp Gln Ile His Glu Thr Lys Arg His Glu Val
 145 150 155 160

Leu Thr Thr Thr Ala Phe Leu Ala Glu Asp Phe Asn Pro Glu Glu Ile
 165 170 175

Asn Leu Asp Cys Thr Asn Pro Arg Tyr Leu Ala Ala Gly Ser Ser Asn
 180 185 190

Ala Val Lys Leu Ser Arg Phe Phe Asp Lys Val Ile Glu Lys Arg Tyr
 195 200 205

Protein Complexes associated with APP-processing
 Phe Leu Arg Glu Gly Asn Gln Ile Pro Gly Phe Pro Asp Arg Lys Arg
 210 215 220

Phe Gly Ala Gly Thr Leu Lys Ser Leu His Tyr Asp
 225 230 235

<210> 168

<211> 457

<212> PRT

<213> Homo sapiens

<400> 168

Met Arg Arg Leu Thr Arg Arg Leu Val Leu Pro Val Phe Gly Val Leu
 1 5 10 15

Trp Ile Thr Val Leu Leu Phe Phe Trp Val Thr Lys Arg Lys Leu Glu
 20 25 30

Val Pro Thr Gly Pro Glu Val Gln Thr Pro Lys Pro Ser Asp Ala Asp
 35 40 45

Trp Asp Asp Leu Trp Asp Gln Phe Asp Glu Arg Arg Tyr Leu Asn Ala
 50 55 60

Lys Lys Trp Arg Val Gly Asp Asp Pro Tyr Lys Leu Tyr Ala Phe Asn
 65 70 75 80

Gln Arg Glu Ser Glu Arg Ile Ser Ser Asn Arg Ala Ile Pro Asp Thr
 85 90 95

Arg His Leu Ser Val Leu Asn Arg Thr Pro Thr His Leu Ile Arg Glu
 100 105 110

Ile Ile Leu Val Asp Asp Phe Ser Asn Asp Pro Asp Asp Cys Lys Gln
 115 120 125

Leu Ile Lys Leu Pro Lys Val Lys Cys Leu Arg Asn Asn Glu Arg Gln
 130 135 140

Gly Leu Val Arg Ser Arg Ile Arg Gly Ala Asp Ile Ala Gln Gly Thr
 145 150 155 160

Thr Leu Thr Phe Leu Asp Ser His Cys Glu Val Asn Arg Asp Trp Leu
 165 170 175

Gln Pro Leu Leu His Arg Val Lys Glu Asp Tyr Thr Arg Val Val Cys
 180 185 190

Protein Complexes associated with APP-processing
 Pro Val Ile Asp Ile Ile Asn Leu Asp Thr Phe Thr Tyr Ile Glu Ser
 195 200 205

Ala Ser Glu Leu Arg Gly Gly Phe Asp Trp Ser Leu His Phe Gln Trp
 210 215 220

Glu Gln Leu Ser Pro Glu Gln Lys Ala Arg Arg Leu Asp Pro Thr Glu
 225 230 235 240

Pro Ile Arg Thr Pro Ile Ile Ala Gly Gly Leu Phe Val Ile Asp Lys
 245 250 255

Ala Trp Phe Asp Tyr Leu Gly Lys Tyr Asp Met Asp Met Asp Ile Trp
 260 265 270

Gly Gly Glu Asn Phe Glu Ile Ser Phe Arg Val Trp Met Cys Gly Gly
 275 280 285

Ser Leu Glu Ile Val Pro Cys Ser Arg Val Gly His Val Phe Arg Lys
 290 295 300

Lys His Pro Tyr Val Phe Pro Asp Gly Asn Ala Asn Thr Tyr Ile Lys
 305 310 315 320

Asn Thr Lys Arg Thr Ala Glu Val Trp Met Asp Glu Tyr Lys Arg Tyr
 325 330 335

Tyr Tyr Ala Ala Arg Pro Phe Ala Leu Glu Arg Pro Phe Gly Asn Val
 340 345 350

Glu Ser Arg Leu Asp Leu Arg Lys Asn Leu Arg Cys Gln Ser Phe Lys
 355 360 365

Trp Tyr Leu Glu Asn Ile Tyr Pro Glu Leu Ser Ile Pro Lys Glu Ser
 370 375 380

Ser Ile Gln Lys Gly Asn Ile Arg Gln Arg Gln Lys Cys Leu Glu Ser
 385 390 395 400

Gln Ala Asn Gly Thr Thr Gly Ser Ser Gly Gln Arg Pro Ala Gly Gly
 405 410 415

Thr Ser Glu Ile Trp Val Gln Lys Pro Arg Val Arg Asn Arg Arg His
 420 425 430

Ala Ala Pro Gln Gly Phe Asp Pro Gly Ala Lys Pro Ser Gln His Trp
 435 440 445

Arg Arg Pro Glu His Pro Ala Ala Glu
 450 455

Protein Complexes associated with APP-processing

<210> 169

<211> 427

<212> PRT

<213> Homo sapiens

<400> 169

Met Phe Phe Ser Met Gly Phe Ile Val Ala Val Lys Gly Lys Ile Ala
 1 5 10 15

Ser Pro Leu Glu Ala Pro Val Phe Val Ala Ala Pro His Ser Thr Phe
 20 25 30

Phe Asp Gly Ile Ala Cys Val Val Ala Gly Leu Pro Ser Met Val Ser
 35 40 45

Arg Asn Glu Asn Ala Gln Val Pro Leu Ile Gly Arg Leu Leu Arg Ala
 50 55 60

Val Gln Pro Val Leu Val Ser Arg Val Asp Pro Asp Ser Arg Lys Asn
 65 70 75 80

Thr Ile Asn Glu Ile Ile Lys Arg Thr Thr Ser Gly Gly Glu Trp Pro
 85 90 95

Gln Ile Leu Val Phe Pro Glu Gly Thr Cys Thr Asn Arg Ser Cys Leu
 100 105 110

Ile Thr Phe Lys Pro Gly Ala Phe Ile Pro Gly Val Pro Val Gln Pro
 115 120 125

Val Leu Leu Arg Tyr Pro Asn Lys Leu Asp Thr Val Thr Trp Thr Trp
 130 135 140

Gln Gly Tyr Thr Phe Ile Gln Leu Cys Met Leu Thr Phe Cys Gln Leu
 145 150 155 160

Phe Thr Lys Val Glu Val Glu Phe Met Pro Val Gln Val Pro Asn Asp
 165 170 175

Glu Glu Lys Asn Asp Pro Val Leu Phe Ala Asn Lys Val Arg Asn Leu
 180 185 190

Met Ala Glu Ala Leu Gly Ile Pro Val Thr Asp His Thr Tyr Glu Asp
 195 200 205

Cys Arg Leu Met Ile Ser Ala Gly Gln Leu Thr Leu Pro Met Glu Ala
 210 215 220

Protein Complexes associated with APP-processing

Gly Leu Val Glu Phe Thr Lys Ile Ser Arg Lys Leu Lys Leu Asp Trp
 225 230 235 240

Asp Gly Val Arg Lys His Leu Asp Glu Tyr Ala Ser Ile Ala Ser Ser
 245 250 255

Ser Lys Gly Gly Arg Ile Gly Ile Glu Glu Phe Ala Lys Tyr Leu Lys
 260 265 270

Leu Pro Val Ser Asp Val Leu Arg Gln Leu Phe Ala Leu Phe Asp Arg
 275 280 285

Asn His Asp Gly Ser Ile Asp Phe Arg Glu Tyr Val Ile Gly Leu Ala
 290 295 300

Val Leu Cys Asn Pro Ser Asn Thr Glu Glu Ile Ile Gln Val Ala Phe
 305 310 315 320

Lys Leu Phe Asp Val Asp Glu Asp Gly Tyr Ile Thr Glu Glu Glu Phe
 325 330 335

Ser Thr Ile Leu Gln Ala Ser Leu Gly Val Pro Asp Leu Asp Val Ser
 340 345 350

Gly Leu Phe Lys Glu Ile Ala Gln Gly Asp Ser Ile Ser Tyr Glu Glu
 355 360 365

Phe Lys Ser Phe Ala Leu Lys His Pro Glu Tyr Ala Lys Ile Phe Thr
 370 375 380

Thr Tyr Leu Asp Leu Gln Thr Cys His Val Phe Ser Leu Pro Lys Glu
 385 390 395 400

Val Gln Thr Thr Pro Ser Thr Ala Ser Asn Lys Val Ser Pro Glu Lys
 405 410 415

His Glu Glu Ser Thr Ser Asp Lys Lys Asp Asp
 420 425

<210> 170

<211> 151

<212> PRT

<213> Homo sapiens

<400> 170

Met Arg Pro Arg Arg Pro His Gln Ile Ala Asp Leu Phe Arg Pro Lys
 1 5 10 15

Protein Complexes associated with APP-processing
 Cys Asn Ser Ser Gln Glu Trp Lys Arg Leu Gly Val Glu Gln Leu Arg
 85 90 95

Leu Ser Thr Val Asp Met Thr Gly Ile Pro Thr Leu Asp Asn Leu Gln
 100 105 110

Lys Gly Val Gln Phe Ala Leu Lys Tyr Gln Ser Leu Gly Gln Cys Val
 115 120 125

Tyr Val His Cys Lys Ala Gly Arg Ser Arg Ser Ala Thr Met Val Ala
 130 135 140

Ala Tyr Leu Ile Gln Val His Lys Trp Ser Pro Glu Glu Ala Val Arg
 145 150 155 160

Ala Ile Ala Lys Ile Arg Ser Tyr Ile His Ile Arg Pro Gly Gln Leu
 165 170 175

Asp Val Leu Lys Glu Phe His Lys Gln Ile Thr Ala Arg Ala Thr Lys
 180 185 190

Asp Gly Thr Phe Val Ile Ser Lys Thr
 195 200

<210> 172

<211> 275

<212> PRT

<213> Homo sapiens

<400> 172

Met Ser Ser Phe Gly Tyr Arg Thr Leu Thr Val Ala Leu Phe Thr Leu
 1 5 10 15

Ile Cys Cys Pro Gly Ser Asp Glu Lys Val Phe Glu Val His Val Arg
 20 25 30

Pro Lys Lys Leu Ala Val Glu Pro Lys Gly Ser Leu Glu Val Asn Cys
 35 40 45

Ser Thr Thr Cys Asn Gln Pro Glu Val Gly Gly Leu Glu Thr Ser Leu
 50 55 60

Asn Lys Ile Leu Leu Asp Glu Gln Ala Gln Trp Lys His Tyr Leu Val
 65 70 75 80

Ser Asn Ile Ser His Asp Thr Val Leu Gln Cys His Phe Thr Cys Ser
 85 90 95

Protein Complexes associated with APP-processing
 Gly Lys Gln Glu Ser Met Asn Ser Asn Val Ser Val Tyr Gln Pro Pro
 100 105 110

Arg Gln Val Ile Leu Thr Leu Gln Pro Thr Leu Val Ala Val Gly Lys
 115 120 125

Ser Phe Thr Ile Glu Cys Arg Val Pro Thr Val Glu Pro Leu Asp Ser
 130 135 140

Leu Thr Leu Phe Leu Phe Arg Gly Asn Glu Thr Leu His Tyr Glu Thr
 145 150 155 160

Phe Gly Lys Ala Ala Pro Ala Pro Gln Glu Ala Thr Ala Thr Phe Asn
 165 170 175

Ser Thr Ala Asp Arg Glu Asp Gly His Arg Asn Phe Ser Cys Leu Ala
 180 185 190

Val Leu Asp Leu Met Ser Arg Gly Gly Asn Ile Phe His Lys His Ser
 195 200 205

Ala Pro Lys Met Leu Glu Ile Tyr Glu Pro Val Ser Asp Ser Gln Met
 210 215 220

Val Ile Ile Val Thr Val Val Ser Val Leu Leu Ser Leu Phe Val Thr
 225 230 235 240

Ser Val Leu Leu Cys Phe Ile Phe Gly Gln His Leu Arg Gln Gln Arg
 245 250 255

Met Gly Thr Tyr Gly Val Arg Ala Ala Trp Arg Arg Leu Pro Gln Ala
 260 265 270

Phe Arg Pro
 275

<210> 173

<211> 336

<212> PRT

<213> Homo sapiens

<400> 173

Ala Ser Gly Glu Trp Arg Val Ser Gly Gly Arg Pro Ala Gly Ala Gly
 1 5 10 15

Arg Pro Glu Glu Ala Leu Ala Ala Gly Ser Asp Pro Arg Gly Ala Ala
 20 25 30

Protein Complexes associated with APP-processing
Ala Arg Leu Ala Cys Ser Ala Pro Thr Pro Gly Gly Gly Thr Met Pro
35 40 45

Thr Glu Arg Arg Gln Pro Leu Tyr Arg Phe Ile Thr Thr Ile Cys Ala
290 295 300

Protein Complexes associated with APP-processing
 Ile Ile Gly Gly Thr Phe Thr Val Ala Gly Ile Leu Asp Ser Cys Ile
 305 310 315 320

Phe Thr Ala Ser Glu Ala Trp Lys Lys Ile Gln Leu Gly Lys Met His
 325 330 335

<210> 174

<211> 651

<212> PRT

<213> Homo sapiens

<400> 174

Asn Ser Lys Lys Met Gln Ser Trp Tyr Ser Met Leu Ser Pro Thr Tyr
 1 5 10 15

Lys Gln Arg Asn Glu Asp Phe Arg Lys Leu Phe Ser Lys Leu Pro Glu
 20 25 30

Ala Glu Arg Leu Ile Val Asp Tyr Ser Cys Ala Leu Gln Arg Glu Ile
 35 40 45

Leu Leu Gln Gly Arg Leu Tyr Leu Ser Glu Asn Trp Ile Cys Phe Tyr
 50 55 60

Ser Asn Ile Phe Arg Trp Glu Thr Thr Ile Ser Ile Gln Leu Lys Glu
 65 70 75 80

Val Thr Cys Leu Lys Lys Glu Lys Thr Ala Lys Leu Ile Pro Asn Ala
 85 90 95

Ile Gln Ile Cys Thr Glu Ser Glu Lys His Phe Phe Thr Ser Phe Gly
 100 105 110

Ala Arg Asp Arg Cys Phe Leu Leu Ile Phe Arg Leu Trp Gln Asn Ala
 115 120 125

Leu Leu Glu Lys Thr Leu Ser Pro Arg Glu Leu Trp His Leu Val His
 130 135 140

Gln Cys Tyr Gly Ser Glu Leu Gly Leu Thr Ser Glu Asp Glu Asp Tyr
 145 150 155 160

Val Ser Pro Leu Gln Leu Asn Gly Leu Gly Thr Pro Lys Glu Val Gly
 165 170 175

Asp Val Ile Ala Leu Ser Asp Ile Thr Ser Ser Gly Ala Ala Asp Arg
 180 185 190

Protein Complexes associated with APP-processing
 Ser Gln Glu Pro Ser Pro Val Gly Ser Arg Arg Gly His Val Thr Pro
 195 200 205

Asn Leu Ser Arg Ala Ser Ser Asp Ala Asp His Gly Ala Glu Glu Asp
 210 215 220

Lys Glu Glu Gln Val Asp Ser Gln Pro Asp Ala Ser Ser Ser Gln Thr
 225 230 235 240

Val Thr Pro Val Ala Glu Pro Pro Ser Thr Glu Pro Thr Gln Pro Asp
 245 250 255

Gly Pro Thr Thr Leu Gly Pro Leu Asp Leu Leu Pro Ser Glu Glu Leu
 260 265 270

Leu Thr Asp Thr Ser Asn Ser Ser Ser Thr Gly Glu Glu Ala Asp
 275 280 285

Leu Ala Ala Leu Leu Pro Asp Leu Ser Gly Arg Leu Leu Ile Asn Ser
 290 295 300

Val Phe His Val Gly Ala Glu Arg Leu Gln Gln Met Leu Phe Ser Asp
 305 310 315 320

Ser Pro Phe Leu Gln Gly Phe Leu Gln Gln Cys Lys Phe Thr Asp Val
 325 330 335

Thr Leu Ser Pro Trp Ser Gly Asp Ser Lys Cys His Gln Arg Arg Val
 340 345 350

Leu Thr Tyr Thr Ile Pro Ile Ser Asn Pro Leu Gly Pro Lys Ser Ala
 355 360 365

Ser Val Val Glu Thr Gln Thr Leu Phe Arg Arg Gly Pro Gln Ala Gly
 370 375 380

Gly Cys Val Val Asp Ser Glu Val Leu Thr Gln Gly Ile Pro Tyr Gln
 385 390 395 400

Asp Tyr Phe Tyr Thr Ala His Arg Tyr Cys Ile Leu Gly Leu Ala Arg
 405 410 415

Asn Lys Ala Arg Leu Arg Val Ser Ser Glu Ile Arg Tyr Arg Lys Gln
 420 425 430

Pro Trp Ser Leu Val Lys Ser Leu Ile Glu Lys Asn Ser Trp Ser Gly
 435 440 445

Ile Glu Asp Tyr Phe His His Leu Glu Arg Glu Leu Ala Lys Ala Glu
 450 455 460

Protein Complexes associated with APP-processing
 Lys Leu Ser Leu Glu Glu Gly Gly Lys Asp Ala Arg Gly Leu Leu Ser
 465 470 475 480

Gly Leu Arg Arg Arg Lys Arg Pro Leu Ser Trp Arg Ala His Gly Asp
 485 490 495

Gly Pro Gln His Pro Asp Pro Asp Pro Cys Ala Arg Ala Gly Ile His
 500 505 510

Thr Ser Gly Ser Leu Ser Ser Arg Phe Ser Glu Pro Ser Val Asp Gln
 515 520 525

Gly Pro Gly Ala Gly Ile Pro Ser Ala Leu Val Leu Ile Ser Ile Val
 530 535 540

Ser Leu Ile Ile Leu Ile Ala Leu Asn Val Leu Leu Phe Tyr Arg Leu
 545 550 555 560

Trp Ser Leu Glu Arg Thr Ala His Thr Phe Glu Ser Trp His Ser Leu
 565 570 575

Ala Leu Ala Lys Gly Lys Phe Pro Gln Thr Ala Thr Glu Trp Ala Glu
 580 585 590

Ile Leu Ala Leu Gln Lys Gln Phe His Ser Val Glu Val His Lys Trp
 595 600 605

Arg Gln Ile Leu Arg Ala Ser Val Glu Leu Leu Asp Glu Met Lys Phe
 610 615 620

Ser Leu Glu Lys Leu His Gln Gly Ile Thr Val Ser Asp Pro Pro Phe
 625 630 635 640

Asp Thr Gln Pro Arg Pro Asp Asp Ser Phe Ser
 645 650

<210> 175

<211> 208

<212> PRT

<213> Homo sapiens

<400> 175

Met Leu Gly Leu Leu Val Ala Leu Leu Ala Leu Gly Leu Ala Val Phe
 1 5 10 15

Ala Leu Leu Asp Val Trp Tyr Leu Val Arg Leu Pro Cys Ala Val Leu
 20 25 30

Protein Complexes associated with APP-processing

Arg Ala Arg Leu Leu Gln Pro Arg Val Arg Asp Leu Leu Ala Glu Gln
 35 40 45

Arg Phe Pro Gly Arg Val Leu Pro Ser Asp Leu Asp Leu Leu Leu His
 50 55 60

Met Asn Asn Ala Arg Tyr Leu Arg Glu Ala Asp Phe Ala Arg Val Ala
 65 70 75 80

His Leu Thr Arg Cys Gly Val Leu Gly Ala Leu Arg Glu Leu Arg Ala
 85 90 95

His Thr Val Leu Ala Ala Ser Cys Ala Arg His Arg Arg Ser Leu Arg
 100 105 110

Leu Leu Glu Pro Phe Glu Val Arg Thr Arg Leu Leu Gly Trp Asp Asp
 115 120 125

Arg Ala Phe Tyr Leu Glu Ala Arg Phe Val Ser Leu Arg Asp Gly Phe
 130 135 140

Val Cys Ala Leu Leu Arg Phe Arg Gln His Leu Leu Gly Thr Ser Pro
 145 150 155 160

Glu Arg Val Val Gln His Leu Cys Gln Arg Arg Val Glu Pro Pro Glu
 165 170 175

Leu Pro Ala Asp Leu Gln His Trp Ile Ser Tyr Asn Glu Ala Ser Ser
 180 185 190

Gln Leu Leu Arg Met Glu Ser Gly Leu Ser Asp Val Thr Lys Asp Gln
 195 200 205

<210> 176

<211> 875

<212> PRT

<213> Homo sapiens

<400> 176

Met Thr Leu Ala Arg Phe Val Leu Ala Leu Met Leu Gly Ala Leu Pro
 1 5 10 15

Glu Val Val Gly Phe Asp Ser Val Leu Asn Asp Ser Leu His His Ser
 20 25 30

His Arg His Ser Pro Pro Ala Gly Pro His Tyr Pro Tyr Tyr Leu Pro
 35 40 45

Protein Complexes associated with APP-processing

Thr Gln Gln Arg Pro Pro Thr Thr Arg Pro Pro Pro Pro Leu Pro Arg
50 55 60

Phe Pro Arg Pro Pro Arg Ala Leu Pro Ala Gln Arg Pro His Ala Leu
65 70 75 80

Gln Ala Gly His Thr Pro Arg Pro His Pro Trp Gly Cys Pro Ala Gly
85 90 95

Glu Pro Trp Val Ser Val Thr Asp Phe Gly Ala Pro Cys Leu Arg Trp
100 105 110

Ala Glu Val Pro Pro Phe Leu Glu Arg Ser Pro Pro Ala Ser Trp Ala
115 120 125

Gln Leu Arg Gly Gln Arg His Asn Phe Cys Arg Ser Pro Asp Gly Ala
130 135 140

Gly Arg Pro Trp Cys Phe Tyr Gly Asp Ala Arg Gly Lys Val Asp Trp
145 150 155 160

Gly Tyr Cys Asp Cys Arg His Gly Ser Val Arg Leu Arg Gly Gly Lys
165 170 175

Asn Glu Phe Glu Gly Thr Val Glu Val Tyr Ala Ser Gly Val Trp Gly
180 185 190

Thr Val Cys Ser Ser His Trp Asp Asp Ser Asp Ala Ser Val Ile Cys
195 200 205

His Gln Leu Gln Leu Gly Gly Lys Gly Ile Ala Lys Gln Thr Pro Phe
210 215 220

Ser Gly Leu Gly Leu Ile Pro Ile Tyr Trp Ser Asn Val Arg Cys Arg
225 230 235 240

Gly Asp Glu Glu Asn Ile Leu Leu Cys Glu Lys Asp Ile Trp Gln Gly
245 250 255

Gly Val Cys Pro Gln Lys Met Ala Ala Ala Val Thr Cys Ser Phe Ser
260 265 270

His Gly Pro Thr Phe Pro Ile Ile Arg Leu Ala Gly Gly Ser Ser Val
275 280 285

His Glu Gly Arg Val Glu Leu Tyr His Ala Gly Gln Trp Gly Thr Val
290 295 300

Cys Asp Asp Gln Trp Asp Asp Ala Asp Ala Glu Val Ile Cys Arg Gln
305 310 315 320

Protein Complexes associated with APP-processing

Leu Gly Leu Ser Gly Ile Ala Lys Ala Trp His Gln Ala Tyr Phe Gly
 325 330 335

Glu Gly Ser Gly Pro Val Met Leu Asp Glu Val Arg Cys Thr Gly Asn
 340 345 350

Glu Leu Ser Ile Glu Gln Cys Pro Lys Ser Ser Trp Gly Glu His Asn
 355 360 365

Cys Gly His Lys Glu Asp Ala Gly Val Ser Cys Thr Pro Leu Thr Asp
 370 375 380

Gly Val Ile Arg Leu Ala Gly Gly Lys Gly Ser His Glu Gly Arg Leu
 385 390 395 400

Glu Val Tyr Tyr Arg Gly Gln Trp Gly Thr Val Cys Asp Asp Gly Trp
 405 410 415

Thr Glu Leu Asn Thr Tyr Val Val Cys Arg Gln Leu Gly Phe Lys Tyr
 420 425 430

Gly Lys Gln Ala Ser Ala Asn His Phe Glu Glu Ser Thr Gly Pro Ile
 435 440 445

Trp Leu Asp Asp Val Ser Cys Ser Gly Lys Glu Thr Arg Phe Leu Gln
 450 455 460

Cys Ser Arg Arg Gln Trp Gly Arg His Asp Cys Ser His Arg Glu Asp
 465 470 475 480

Val Ser Ile Ala Cys Tyr Pro Gly Gly Glu Gly His Arg Leu Ser Leu
 485 490 495

Gly Phe Pro Val Arg Leu Met Asp Gly Glu Asn Lys Lys Glu Gly Arg
 500 505 510

Val Glu Val Phe Ile Asn Gly Gln Trp Gly Thr Ile Cys Asp Asp Gly
 515 520 525

Trp Thr Asp Lys Asp Ala Ala Val Ile Cys Arg Gln Leu Gly Tyr Lys
 530 535 540

Gly Pro Ala Arg Ala Arg Thr Met Ala Tyr Phe Gly Glu Gly Lys Gly
 545 550 555 560

Pro Ile His Val Asp Asn Val Lys Cys Thr Gly Asn Glu Arg Ser Leu
 565 570 575

Ala Asp Cys Ile Lys Gln Asp Ile Gly Arg His Asn Cys Arg His Ser
 580 585 590

Protein Complexes associated with APP-processing

Glu Asp Ala Gly Val Ile Cys Asp Tyr Phe Gly Lys Lys Ala Ser Gly
595 600 605

Asn Ser Asn Lys Glu Ser Leu Ser Ser Val Cys Gly Leu Arg Leu Leu
610 615 620

His Arg Arg Gln Lys Arg Ile Ile Gly Gly Lys Asn Ser Leu Arg Gly
625 630 635 640

Gly Trp Pro Trp Gln Val Ser Leu Arg Leu Lys Ser Ser His Gly Asp
645 650 655

Gly Arg Leu Leu Cys Gly Ala Thr Leu Leu Ser Ser Cys Trp Val Leu
660 665 670

Thr Ala Ala His Cys Phe Lys Arg Tyr Gly Asn Ser Thr Arg Ser Tyr
675 680 685

Ala Val Arg Val Gly Asp Tyr His Thr Leu Val Pro Glu Glu Phe Glu
690 695 700

Glu Glu Ile Gly Val Gln Gln Ile Val Ile His Arg Glu Tyr Arg Pro
705 710 715 720

Asp Arg Ser Asp Tyr Asp Ile Ala Leu Val Arg Leu Gln Gly Pro Glu
725 730 735

Glu Gln Cys Ala Arg Phe Ser Ser His Val Leu Pro Ala Cys Leu Pro
740 745 750

Leu Trp Arg Glu Arg Pro Gln Lys Thr Ala Ser Asn Cys Tyr Ile Thr
755 760 765

Gly Trp Gly Asp Thr Gly Arg Ala Tyr Ser Arg Thr Leu Gln Gln Ala
770 775 780

Ala Ile Pro Leu Leu Pro Lys Arg Phe Cys Glu Glu Arg Tyr Lys Gly
785 790 795 800

Arg Phe Thr Gly Arg Met Leu Cys Ala Gly Asn Leu His Glu His Lys
805 810 815

Arg Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Met Cys Glu
820 825 830

Arg Pro Gly Glu Ser Trp Val Val Tyr Gly Val Thr Ser Trp Gly Tyr
835 840 845

Gly Cys Gly Val Lys Asp Ser Pro Gly Val Tyr Thr Lys Val Ser Ala
850 855 860

Protein Complexes associated with APP-processing

Phe Val Pro Trp Ile Lys Ser Val Thr Lys Leu
 865 870 875

<210> 177

<211> 713

<212> PRT

<213> Homo sapiens

<400> 177

Met Glu Pro Gly Thr Gly Gly Ser Arg Lys Arg Leu Gly Pro Arg Ala
 1 5 10 15

Gly Phe Arg Phe Trp Pro Pro Phe Phe Pro Arg Arg Ser Gln Ala Gly
 20 25 30

Ser Ser Lys Phe Pro Thr Pro Leu Gly Pro Glu Asn Ser Gly Asn Pro
 35 40 45

Thr Leu Leu Ser Ser Ala Gln Pro Glu Thr Arg Val Ser Tyr Trp Thr
 50 55 60

Lys Leu Leu Ser Gln Leu Leu Ala Pro Leu Pro Gly Leu Leu Gln Lys
 65 70 75 80

Val Leu Ile Trp Ser Gln Leu Phe Gly Gly Met Phe Pro Thr Arg Trp
 85 90 95

Leu Asp Phe Ala Gly Val Tyr Ser Ala Leu Arg Ala Leu Lys Gly Arg
 100 105 110

Glu Lys Pro Ala Ala Pro Thr Ala Gln Lys Ser Leu Ser Ser Leu Gln
 115 120 125

Leu Asp Ser Ser Asp Pro Ser Val Thr Ser Pro Leu Asp Trp Leu Glu
 130 135 140

Glu Gly Ile His Trp Gln Tyr Ser Pro Pro Asp Leu Lys Leu Glu Leu
 145 150 155 160

Lys Ala Lys Gly Ser Ala Leu Asp Pro Ala Ala Gln Ala Phe Leu Leu
 165 170 175

Glu Gln Gln Leu Trp Gly Val Glu Leu Leu Pro Ser Ser Leu Gln Ser
 180 185 190

Arg Leu Tyr Ser Asn Arg Glu Leu Gly Ser Ser Pro Ser Gly Pro Leu
 195 200 205

Protein Complexes associated with APP-processing

Asn Ile Gln Arg Ile Asp Asp Phe Ser Val Val Ser Tyr Leu Leu Asn
 210 215 220

Pro Ser Tyr Leu Asp Cys Phe Pro Arg Leu Glu Val Ser Tyr Gln Asn
 225 230 235 240

Ser Asp Gly Asn Ser Glu Val Val Gly Phe Gln Thr Leu Thr Pro Glu
 245 250 255

Ser Ser Cys Leu Arg Glu Asp His Cys His Pro Gln Pro Leu Ser Ala
 260 265 270

Glu Leu Ile Pro Ala Ser Trp Gln Gly Cys Pro Pro Leu Ser Thr Glu
 275 280 285

Gly Leu Pro Glu Ile His His Leu Arg Met Lys Arg Leu Glu Phe Leu
 290 295 300

Gln Gln Ala Ser Lys Gly Gln Asp Leu Pro Thr Pro Asp Gln Asp Asn
 305 310 315 320

Gly Tyr His Ser Leu Glu Glu Glu His Ser Leu Leu Arg Met Asp Pro
 325 330 335

Lys His Cys Arg Asp Asn Pro Thr Gln Phe Val Pro Ala Ala Gly Asp
 340 345 350

Ile Pro Gly Asn Thr Gln Glu Ser Thr Glu Glu Lys Ile Glu Leu Leu
 355 360 365

Thr Thr Glu Val Pro Leu Ala Leu Glu Glu Glu Ser Pro Ser Glu Gly
 370 375 380

Cys Pro Ser Ser Glu Ile Pro Met Glu Lys Glu Pro Gly Glu Gly Arg
 385 390 395 400

Ile Ser Val Val Asp Tyr Ser Tyr Leu Glu Gly Asp Leu Pro Ile Ser
 405 410 415

Ala Arg Pro Ala Cys Ser Asn Lys Leu Ile Asp Tyr Ile Leu Gly Gly
 420 425 430

Ala Ser Ser Asp Leu Glu Thr Ser Ser Asp Pro Glu Gly Glu Asp Trp
 435 440 445

Asp Glu Glu Ala Glu Asp Asp Gly Phe Asp Ser Asp Ser Ser Leu Ser
 450 455 460

Asp Ser Asp Leu Glu Gln Asp Pro Glu Gly Leu His Leu Trp Asn Ser
 465 470 475 480

Phe Cys Ser Val Asp Pro Tyr Asn Pro Gln Asn Phe Thr Ala Thr Ile
485 490 495

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Protein Complexes associated with APP-processing

<400> 178

Met Ala Ala Glu Thr Leu Leu Ser Ser Leu Leu Gly Leu Leu Leu Leu
 1 5 10 15
 Gly Leu Leu Leu Pro Ala Ser Leu Thr Gly Gly Val Gly Ser Leu Asn
 20 25 30
 Leu Glu Glu Leu Ser Glu Met Arg Tyr Gly Ile Glu Ile Leu Pro Leu
 35 40 45
 Pro Val Met Gly Gly Gln Ser Gln Ser Ser Asp Val Val Ile Val Ser
 50 55 60
 Ser Lys Tyr Lys Gln Arg Tyr Glu Cys Arg Leu Pro Ala Gly Ala Ile
 65 70 75 80
 His Phe Gln Arg Glu Arg Glu Glu Glu Thr Pro Ala Tyr Gln Gly Pro
 85 90 95
 Gly Ile Pro Glu Leu Leu Ser Pro Met Arg Asp Ala Pro Cys Leu Leu
 100 105 110
 Lys Thr Lys Asp Trp Trp Thr Tyr Glu Phe Cys Tyr Gly Arg His Ile
 115 120 125
 Gln Gln Tyr His Met Glu Asp Ser Glu Ile Lys Gly Glu Val Leu Tyr
 130 135 140
 Leu Gly Tyr Tyr Gln Ser Ala Phe Asp Trp Asp Asp Glu Thr Ala Lys
 145 150 155 160
 Ala Ser Lys Gln His Arg Leu Lys Arg Tyr His Ser Gln Thr Tyr Gly
 165 170 175
 Asn Gly Ser Lys Cys Asp Leu Asn Gly Arg Pro Arg Glu Ala Glu Val
 180 185 190
 Arg Phe Leu Cys Asp Glu Gly Ala Gly Ile Ser Gly Asp Tyr Ile Asp
 195 200 205
 Arg Val Asp Glu Pro Leu Ser Cys Ser Tyr Val Leu Thr Ile Arg Thr
 210 215 220
 Pro Arg Leu Cys Pro His Pro Leu Leu Arg Pro Pro Pro Ser Ala Ala
 225 230 235 240
 Pro Gln Ala Ile Leu Cys His Pro Ser Leu Gln Pro Glu Glu Tyr Met
 245 250 255

Protein Complexes associated with APP-processing
 Ala Tyr Val Gln Arg Gln Ala Asp Ser Lys Gln Tyr Gly Asp Lys Ile
 260 265 270

Ile Glu Glu Leu Gln Asp Leu Gly Pro Gln Val Trp Ser Glu Thr Lys
 275 280 285

Ser Gly Val Ala Pro Gln Lys Met Ala Gly Ala Ser Pro Thr Lys Asp
 290 295 300

Asp Ser Lys Asp Ser Asp Phe Trp Lys Met Leu Asn Glu Pro Glu Asp
 305 310 315 320

Gln Ala Pro Gly Gly Glu Glu Val Pro Ala Glu Glu Gln Asp Pro Ser
 325 330 335

Pro Glu Ala Ala Asp Ser Ala Ser Gly Ala Pro Asn Asp Phe Gln Asn
 340 345 350

Asn Val Gln Val Lys Val Ile Arg Ser Pro Ala Asp Leu Ile Arg Phe
 355 360 365

Ile Glu Glu Leu Lys Gly Gly Thr Lys Lys Gly Lys Pro Asn Ile Gly
 370 375 380

Gln Glu Gln Pro Val Asp Asp Ala Ala Glu Val Pro Gln Arg Glu Pro
 385 390 395 400

Glu Lys Glu Arg Gly Asp Pro Glu Arg Gln Arg Glu Met Glu Glu Glu
 405 410 415

Glu Asp Glu Asp Glu Asp Glu Asp Glu Asp Glu Arg Gln Leu
 420 425 430

Leu Gly Glu Phe Glu Lys Glu Leu Glu Gly Ile Leu Leu Pro Ser Asp
 435 440 445

Arg Asp Arg Leu Arg Ser Glu Val Lys Ala Gly Met Glu Arg Glu Leu
 450 455 460

Glu Asn Ile Ile Gln Glu Thr Glu Lys Glu Leu Asp Pro Asp Gly Leu
 465 470 475 480

Lys Lys Glu Ser Glu Arg Asp Arg Ala Met Leu Ala Leu Thr Ser Thr
 485 490 495

Leu Asn Lys Leu Ile Lys Arg Leu Glu Glu Lys Gln Ser Pro Glu Leu
 500 505 510

Val Lys Lys His Lys Lys Lys Arg Val Val Pro Lys Lys Pro Pro Pro
 515 520 525

Protein Complexes associated with APP-processing
 Ser Pro Gln Pro Thr Glu Glu Asp Pro Glu His Arg Val Arg Val Arg
 530 535 540

Val Thr Lys Leu Arg Leu Gly Gly Pro Asn Gln Asp Leu Thr Val Leu
 545 550 555 560

Glu Met Lys Arg Glu Asn Pro Gln Leu Lys Gln Ile Glu Gly Leu Val
 565 570 575

Lys Glu Leu Leu Glu Arg Glu Gly Leu Thr Ala Ala Gly Lys Ile Glu
 580 585 590

Ile Lys Ile Val Arg Pro Trp Ala Glu Gly Thr Glu Glu Gly Ala Arg
 595 600 605

Trp Leu Thr Asp Glu Asp Thr Arg Asn Leu Lys Glu Ile Phe Phe Asn
 610 615 620

Ile Leu Val Pro Gly Ala Glu Glu Ala Gln Lys Glu Arg Gln Arg Gln
 625 630 635 640

Lys Glu Leu Glu Ser Asn Tyr Arg Arg Val Trp Gly Ser Pro Gly Gly
 645 650 655

Glu Gly Thr Gly Asp Leu Asp Glu Phe Asp Phe
 660 665

<210> 179

<211> 211

<212> PRT

<213> Homo sapiens

<400> 179

Met Ala Val Val Pro Leu Leu Leu Leu Gly Gly Leu Trp Ser Ala Val
 1 5 10 15

Gly Ala Ser Ser Leu Gly Val Val Thr Cys Gly Ser Val Val Lys Leu
 20 25 30

Leu Asn Thr Arg His Asn Val Arg Leu His Ser His Asp Val Arg Tyr
 35 40 45

Gly Ser Gly Ser Gly Gln Gln Ser Val Thr Gly Val Thr Ser Val Asp
 50 55 60

Asp Ser Asn Ser Tyr Trp Arg Ile Arg Gly Lys Ser Ala Thr Val Cys
 65 70 75 80

Protein Complexes associated with APP-processing
 Glu Arg Gly Thr Pro Ile Lys Cys Gly Gln Pro Ile Arg Leu Thr His
 85 90 95

Val Asn Thr Gly Arg Asn Leu His Ser His His Phe Thr Ser Pro Leu
 100 105 110

Ser Gly Asn Gln Glu Val Ser Ala Phe Gly Glu Glu Gly Glu Gly Asp
 115 120 125

Tyr Leu Asp Asp Trp Thr Val Leu Cys Asn Gly Pro Tyr Trp Val Arg
 130 135 140

Asp Gly Glu Val Arg Phe Lys His Ser Ser Thr Glu Val Leu Leu Ser
 145 150 155 160

Val Thr Gly Glu Gln Tyr Gly Arg Pro Ile Ser Gly Gln Lys Glu Val
 165 170 175

His Gly Met Ala Gln Pro Ser Gln Asn Asn Tyr Trp Lys Ala Met Glu
 180 185 190

Gly Ile Phe Met Lys Pro Ser Glu Leu Leu Lys Ala Glu Ala His His
 195 200 205

Ala Glu Leu
 210

<210> 180

<211> 801

<212> PRT

<213> Homo sapiens

<400> 180

Met Glu Ala Ser Gly Lys Leu Ile Cys Arg Gln Arg Gln Val Leu Phe
 1 5 10 15

Ser Phe Leu Leu Leu Gly Leu Ser Leu Ala Gly Ala Ala Glu Pro Arg
 20 25 30

Ser Tyr Ser Val Val Glu Glu Thr Glu Gly Ser Ser Phe Val Thr Asn
 35 40 45

Leu Ala Lys Asp Leu Gly Leu Glu Gln Arg Glu Phe Ser Arg Arg Gly
 50 55 60

Val Arg Val Val Ser Arg Gly Asn Lys Leu His Leu Gln Leu Asn Gln
 65 70 75 80

Glu Thr Ala Asp Leu Leu Leu Asn Glu Lys Leu Asp Arg Glu Asp Leu
85 90 95

Ser Pro Phe Glu Phe Phe Gln Ala Glu Leu Gln Val Ile Asp Ile Asn
115 120 125

Glu Ser Ser Pro Pro Gly Thr Ala Phe Pro Leu Lys Asn Ala Glu Asp
145 150 155 160

Ser Tyr Phe Arg Val Leu Thr Arg Lys Arg Ser Asp Gly Arg Lys Tyr
180 185 190

Leu Arg Leu Thr Leu Thr Ala Leu Asp Gly Gly Ser Pro Pro Arg Ser
210 . 215 220 .

Pro Glu Phe Gln Gln Pro Phe Tyr Arg Val Gln Ile Ser Glu Asp Ser
245 250 255

Gly Val Asn Gly Glu Ile Ser Tyr Ser Leu Phe Gln Ala Ser Asp Glu
275 280 285

Lys Lys Gln Leu Asp Phe Glu Lys Phe Gln Ser Tyr Glu Val Asn Ile
305 310 315 320

Gln Val Ile Asp Val Asn Asp His Ala Pro Glu Val Thr Met Ser Ala
340 345 350

Protein Complexes associated with APP-processing

Phe Thr Ser Pro Ile Pro Glu Asn Ala Pro Glu Thr Val Val Ala Leu
 355 360 365

Phe Ser Val Ser Asp Leu Asp Ser Gly Glu Asn Gly Lys Ile Ser Cys
 370 375 380

Ser Ile Gln Glu Asp Leu Pro Phe Leu Leu Lys Ser Ser Val Gly Asn
 385 390 395 400

Phe Tyr Thr Leu Leu Thr Glu Thr Pro Leu Asp Arg Glu Ser Arg Ala
 405 410 415

Glu Tyr Asn Val Thr Ile Thr Val Thr Asp Leu Gly Thr Pro Arg Leu
 420 425 430

Thr Thr His Leu Asn Met Thr Val Leu Val Ser Asp Val Asn Asp Asn
 435 440 445

Ala Pro Ala Phe Thr Gln Thr Ser Tyr Thr Leu Phe Val Arg Glu Asn
 450 455 460

Asn Ser Pro Ala Leu His Ile Gly Ser Val Ser Ala Thr Asp Arg Asp
 465 470 475 480

Ser Gly Thr Asn Ala Gln Val Thr Tyr Ser Leu Leu Pro Pro Gln Asp
 485 490 495

Pro His Leu Pro Leu Ala Ser Leu Val Ser Ile Asn Thr Asp Asn Gly
 500 505 510

His Leu Phe Ala Leu Arg Ser Leu Asp Tyr Glu Ala Leu Gln Ala Phe
 515 520 525

Glu Phe Arg Val Gly Ala Ser Asp Arg Gly Ser Pro Ala Leu Ser Ser
 530 535 540

Glu Ala Leu Val Arg Val Leu Val Leu Asp Ala Asn Asp Asn Ser Pro
 545 550 555 560

Phe Val Leu Tyr Pro Leu Gln Asn Gly Ser Ala Pro Cys Thr Gly Leu
 565 570 575

Val Pro Arg Ala Ala Glu Pro Gly Tyr Leu Val Thr Lys Val Val Ala
 580 585 590

Val Asp Gly Asp Ser Gly Gln Asn Ala Trp Leu Ser Tyr Gln Leu Leu
 595 600 605

Lys Ala Thr Glu Pro Gly Leu Phe Gly Val Trp Ala His Asn Gly Glu
 610 615 620

Protein Complexes associated with APP-processing
 Val Arg Thr Ala Arg Leu Leu Ser Glu Arg Asp Ala Ala Lys Gln Arg
 625 630 635 640

Leu Val Val Leu Val Lys Asp Asn Gly Glu Pro Pro Cys Ser Ala Thr
 645 650 655

Ala Thr Leu His Leu Leu Leu Val Asp Gly Phe Ser Gln Pro Tyr Leu
 660 665 670

Pro Leu Pro Glu Ala Ala Pro Ala Gln Gly Gln Ala Asp Ser Leu Thr
 675 680 685

Val Tyr Leu Val Val Ala Leu Ala Ser Val Ser Ser Leu Phe Leu Phe
 690 695 700

Ser Val Leu Leu Phe Val Ala Val Leu Leu Cys Arg Arg Ser Arg Ala
 705 710 715 720

Ala Ser Val Gly Arg Cys Ser Val Pro Glu Gly Pro Phe Pro Gly His
 725 730 735

Leu Val Asp Val Arg Gly Thr Gly Ser Leu Ser Gln Asn Tyr Gln Tyr
 740 745 750

Glu Val Cys Leu Ala Gly Gly Ser Gly Thr Asn Glu Phe Gln Phe Leu
 755 760 765

Lys Pro Val Leu Pro Asn Ile Gln Gly His Ser Phe Gly Pro Glu Met
 770 775 780

Glu Gln Asn Ser Asn Phe Arg Asn Gly Phe Gly Phe Ser Leu Gln Leu
 785 790 795 800

Lys

<210> 181

<211> 270

<212> PRT

<213> Homo sapiens

<400> 181

Met Ala Ser Arg Gly Val Val Gly Ile Phe Phe Leu Ser Ala Val Pro
 1 5 10 15

Leu Val Cys Leu Glu Leu Arg Arg Gly Ile Pro Asp Ile Gly Ile Lys
 20 25 30

Protein Complexes associated with APP-processing
 Asp Phe Leu Leu Cys Gly Arg Ile Leu Leu Leu Leu Ala Leu Leu
 35 40 45

Thr Leu Ile Ile Ser Val Thr Thr Ser Trp Leu Asn Ser Phe Lys Ser
 50 55 60

Pro Gln Val Tyr Leu Lys Glu Glu Glu Glu Lys Asn Glu Lys Arg Gln
 65 70 75 80

Lys Leu Val Arg Lys Lys Gln Gln Glu Ala Gln Gly Glu Lys Ala Ser
 85 90 95

Arg Tyr Ile Glu Asn Val Leu Lys Pro His Gln Glu Met Lys Leu Arg
 100 105 110

Lys Leu Glu Glu Arg Phe Tyr Gln Met Thr Gly Glu Ala Trp Lys Leu
 115 120 125

Ser Ser Gly His Lys Leu Gly Gly Asp Glu Gly Thr Ser Gln Thr Ser
 130 135 140

Phe Glu Thr Ser Asn Arg Glu Ala Ala Lys Ser Gln Asn Leu Pro Lys
 145 150 155 160

Pro Leu Thr Glu Phe Pro Ser Pro Ala Glu Gln Pro Thr Cys Lys Glu
 165 170 175

Ile Pro Asp Leu Pro Glu Glu Pro Ser Gln Thr Ala Glu Glu Val Val
 180 185 190

Thr Val Ala Leu Arg Cys Pro Ser Gly Asn Val Leu Arg Arg Arg Phe
 195 200 205

Leu Lys Ser Tyr Ser Ser Gln Val Leu Phe Asp Trp Met Thr Arg Ile
 210 215 220

Gly Tyr His Ile Ser Leu Tyr Ser Leu Ser Thr Ser Phe Pro Arg Arg
 225 230 235 240

Pro Leu Ala Val Glu Gly Gly Gln Ser Leu Glu Asp Ile Gly Ile Thr
 245 250 255

Val Asp Thr Val Leu Ile Leu Glu Glu Lys Glu Gln Thr Asn
 260 265 270

<210> 182

<211> 180

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 182

Met Ala Ala Ala Glu Glu Glu Asp Gly Gly Pro Glu Gly Pro Asn Arg
 1 5 10 15
 Glu Arg Gly Gly Ala Gly Ala Thr Phe Glu Cys Asn Ile Cys Leu Glu
 20 25 30
 Thr Ala Arg Glu Ala Val Val Ser Val Cys Gly His Leu Tyr Cys Trp
 35 40 45
 Pro Cys Leu His Gln Trp Leu Glu Thr Arg Pro Glu Arg Gln Glu Cys
 50 55 60
 Pro Val Cys Lys Ala Gly Ile Ser Arg Glu Lys Val Val Pro Leu Tyr
 65 70 75 80
 Gly Arg Gly Ser Gln Lys Pro Gln Asp Pro Arg Leu Lys Thr Pro Pro
 85 90 95
 Arg Pro Gln Gly Gln Arg Pro Ala Pro Glu Ser Arg Gly Gly Phe Gln
 100 105 110
 Pro Phe Gly Asp Thr Gly Gly Phe His Phe Ser Phe Gly Val Gly Ala
 115 120 125
 Phe Pro Phe Gly Phe Phe Thr Thr Val Phe Asn Ala His Glu Pro Phe
 130 135 140
 Arg Arg Gly Thr Gly Val Asp Leu Gly Gln Gly His Pro Ala Ser Ser
 145 150 155 160
 Trp Gln Asp Ser Leu Phe Leu Phe Leu Ala Ile Phe Phe Phe Phe Trp
 165 170 175
 Leu Leu Ser Ile
 180

<210> 183

<211> 300

<212> PRT

<213> Homo sapiens

<400> 183

Met Lys Phe Leu Leu Asp Ile Leu Leu Leu Leu Pro Leu Leu Ile Val
 1 5 10 15

Protein Complexes associated with APP-processing
 Cys Ser Leu Glu Ser Phe Val Lys Leu Phe Ile Pro Lys Arg Arg Lys
 20 25 30

Ser Val Thr Gly Glu Ile Val Leu Ile Thr Gly Ala Gly His Gly Ile
 35 40 45

Gly Arg Leu Thr Ala Tyr Glu Phe Ala Lys Leu Lys Ser Lys Leu Val
 50 55 60

Leu Trp Asp Ile Asn Lys His Gly Leu Glu Glu Thr Ala Ala Lys Cys
 65 70 75 80

Lys Gly Leu Gly Ala Lys Val His Thr Phe Val Val Asp Cys Ser Asn
 85 90 95

Arg Glu Asp Ile Tyr Ser Ser Ala Lys Lys Val Lys Ala Glu Ile Gly
 100 105 110

Asp Val Ser Ile Leu Val Asn Asn Ala Gly Val Val Tyr Thr Ser Asp
 115 120 125

Leu Phe Ala Thr Gln Asp Pro Gln Ile Glu Lys Thr Phe Glu Val Asn
 130 135 140

Val Leu Ala His Phe Trp Thr Thr Lys Ala Phe Leu Pro Ala Met Thr
 145 150 155 160

Lys Asn Asn His Gly His Ile Val Thr Val Ala Ser Ala Ala Gly His
 165 170 175

Val Ser Val Pro Phe Leu Leu Ala Tyr Cys Ser Ser Lys Phe Ala Ala
 180 185 190

Val Gly Phe His Lys Thr Leu Thr Asp Glu Leu Ala Ala Leu Gln Ile
 195 200 205

Thr Gly Val Lys Thr Thr Cys Leu Cys Pro Asn Phe Val Asn Thr Gly
 210 215 220

Phe Ile Lys Asn Pro Ser Thr Ser Leu Gly Pro Thr Leu Glu Pro Glu
 225 230 235 240

Glu Val Val Asn Arg Leu Met His Gly Ile Leu Thr Glu Gln Lys Met
 245 250 255

Ile Phe Ile Pro Ser Ser Ile Ala Phe Leu Thr Thr Leu Glu Arg Ile
 260 265 270

Leu Pro Glu Arg Phe Leu Ala Val Leu Lys Arg Lys Ile Ser Val Lys
 275 280 285

Protein Complexes associated with APP-processing
 Phe Asp Ala Val Ile Gly Tyr Lys Met Lys Ala Gln
 290 295 300

<210> 184

<211> 221

<212> PRT

<213> Homo sapiens

<400> 184

Met Trp Ser Ala Gly Arg Gly Gly Ala Ala Trp Pro Val Leu Leu Gly
 1 5 10 15

Leu Leu Leu Ala Leu Leu Val Pro Gly Gly Gly Ala Ala Lys Thr Gly
 20 25 30

Ala Glu Leu Val Thr Cys Gly Ser Val Leu Lys Leu Leu Asn Thr His
 35 40 45

His Arg Val Arg Leu His Ser His Asp Ile Lys Tyr Gly Ser Gly Ser
 50 55 60

Gly Gln Gln Ser Val Thr Gly Val Glu Ala Ser Asp Asp Ala Asn Ser
 65 70 75 80

Tyr Trp Arg Ile Arg Gly Gly Ser Glu Gly Gly Cys Pro Cys Gly Ser
 85 90 95

Pro Val Arg Cys Gly Gln Ala Val Arg Leu Thr His Val Leu Thr Gly
 100 105 110

Lys Asn Leu His Thr His His Phe Pro Ser Pro Leu Ser Asn Asn Gln
 115 120 125

Glu Val Ser Ala Phe Gly Glu Asp Gly Glu Gly Asp Asp Leu Asp Leu
 130 135 140

Trp Thr Val Arg Cys Ser Gly Gln His Trp Glu Arg Glu Ala Ala Val
 145 150 155 160

Arg Leu Gln His Val Gly Thr Ser Val Phe Leu Ser Val Thr Gly Glu
 165 170 175

Gln Tyr Gly Ser Pro Ile Arg Gly Gln His Glu Val His Gly Met Pro
 180 185 190

Ser Ala Asn Thr His Asn Thr Trp Lys Ala Met Glu Gly Ile Phe Ile
 195 200 205

Protein Complexes associated with APP-processing
 Lys Pro Ser Val Glu Pro Ser Ala Gly His Asp Glu Leu
 210 215 220

<210> 185

<211> 287

<212> PRT

<213> Homo sapiens

<400> 185

Gly Arg Trp Ala Ser Gly Glu Met Ala Pro Ser Gly Ser Leu Ala Val
 1 5 10 15

Pro Leu Ala Val Leu Val Leu Leu Leu Trp Gly Ala Pro Trp Thr His
 20 25 30

Gly Arg Arg Ser Asn Val Arg Val Ile Thr Asp Glu Asn Trp Arg Glu
 35 40 45

Leu Leu Glu Gly Asp Trp Met Ile Glu Phe Tyr Ala Pro Trp Cys Pro
 50 55 60

Ala Cys Gln Asn Leu Gln Pro Glu Trp Glu Ser Phe Ala Glu Trp Gly
 65 70 75 80

Glu Asp Leu Glu Val Asn Ile Ala Lys Val Asp Val Thr Glu Gln Pro
 85 90 95

Gly Leu Ser Gly Arg Phe Ile Ile Thr Ala Leu Pro Thr Ile Tyr His
 100 105 110

Cys Lys Asp Gly Glu Phe Arg Arg Tyr Gln Gly Pro Arg Thr Lys Lys
 115 120 125

Asp Phe Ile Asn Phe Ile Ser Asp Lys Glu Trp Lys Ser Ile Glu Pro
 130 135 140

Val Ser Ser Trp Phe Gly Pro Gly Ser Val Leu Met Ser Ser Met Ser
 145 150 155 160

Ala Leu Phe Gln Leu Ser Met Trp Ile Arg Thr Cys His Asn Tyr Phe
 165 170 175

Ile Glu Asp Leu Gly Leu Pro Val Trp Gly Ser Tyr Thr Val Phe Ala
 180 185 190

Leu Ala Thr Leu Phe Ser Gly Leu Leu Leu Gly Leu Cys Met Ile Phe
 195 200 205

Protein Complexes associated with APP-processing
 Val Ala Asp Cys Leu Cys Pro Ser Lys Arg Arg Arg Pro Gln Pro Tyr
 210 215 220

Pro Tyr Pro Ser Lys Lys Leu Leu Ser Glu Ser Ala Gln Pro Leu Lys
 225 230 235 240

Lys Val Glu Glu Glu Gln Glu Ala Asp Glu Glu Asp Val Ser Glu Glu
 245 250 255

Glu Ala Glu Ser Lys Glu Gly Thr Asn Lys Asp Phe Pro Gln Asn Ala
 260 265 270

Ile Arg Gln Arg Ser Leu Gly Pro Ser Leu Ala Thr Asp Lys Ser
 275 280 285

<210> 186

<211> 282

<212> PRT

<213> Homo sapiens

<400> 186

Ala Val Pro Pro Thr Tyr Ala Asp Leu Gly Lys Ser Ala Arg Asp Val
 1 5 10 15

Phe Thr Lys Gly Tyr Gly Phe Gly Leu Ile Lys Leu Asp Leu Lys Thr
 20 25 30

Lys Ser Glu Asn Gly Leu Glu Phe Thr Ser Ser Gly Ser Ala Asn Thr
 35 40 45

Glu Thr Thr Lys Val Thr Gly Ser Leu Glu Thr Lys Tyr Arg Trp Thr
 50 55 60

Glu Tyr Gly Leu Thr Phe Thr Glu Lys Trp Asn Thr Asp Asn Thr Leu
 65 70 75 80

Gly Thr Glu Ile Thr Val Glu Asp Gln Leu Ala Arg Gly Leu Lys Leu
 85 90 95

Thr Phe Asp Ser Ser Phe Ser Pro Asn Thr Gly Lys Lys Asn Ala Lys
 100 105 110

Ile Lys Thr Gly Tyr Lys Arg Glu His Ile Asn Leu Gly Cys Asp Met
 115 120 125

Asp Phe Asp Ile Ala Gly Pro Ser Ile Arg Gly Ala Leu Val Leu Gly
 130 135 140

Protein Complexes associated with APP-processing

Tyr Glu Gly Trp Leu Ala Gly Tyr Gln Met Asn Phe Glu Thr Ala Lys
 145 150 155 160

Ser Arg Val Thr Gln Ser Asn Phe Ala Val Gly Tyr Lys Thr Asp Glu
 165 170 175

Phe Gln Leu His Thr Asn Val Asn Asp Gly Thr Glu Phe Gly Gly Ser
 180 185 190

Ile Tyr Gln Lys Val Asn Lys Lys Leu Glu Thr Ala Val Asn Leu Ala
 195 200 205

Trp Thr Ala Gly Asn Ser Asn Thr Arg Phe Gly Ile Ala Ala Lys Tyr
 210 215 220

Gln Ile Asp Pro Asp Ala Cys Phe Ser Ala Lys Val Asn Asn Ser Ser
 225 230 235 240

Leu Ile Gly Leu Gly Tyr Thr Gln Thr Leu Lys Pro Gly Ile Lys Leu
 245 250 255

Thr Leu Ser Ala Leu Leu Asp Gly Lys Asn Val Asn Ala Gly Gly His
 260 265 270

Lys Leu Gly Leu Gly Leu Glu Phe Gln Ala
 275 280

<210> 187

<211> 558

<212> PRT

<213> Homo sapiens

<400> 187

Met Ala Lys Asn Arg Arg Asp Arg Asn Ser Trp Gly Gly Phe Ser Glu
 1 5 10 15

Lys Thr Tyr Glu Trp Ser Ser Glu Glu Glu Glu Pro Val Lys Lys Ala
 20 25 30

Gly Pro Val Gln Val Leu Ile Val Lys Asp Asp His Ser Phe Glu Leu
 35 40 45

Asp Glu Thr Ala Leu Asn Arg Ile Leu Leu Ser Glu Ala Val Arg Asp
 50 55 60

Lys Glu Val Val Ala Val Ser Val Ala Gly Ala Phe Arg Lys Gly Lys
 65 70 75 80

Protein Complexes associated with APP-processing

Ser Phe Leu Met Asp Phe Met Leu Arg Tyr Met Tyr Asn Gln Glu Ser
85 90 95

Val Asp Trp Val Gly Asp Tyr Asn Glu Pro Leu Thr Gly Phe Ser Trp
100 105 110

Arg Gly Gly Ser Glu Arg Glu Thr Thr Gly Ile Gln Ile Trp Ser Glu
115 120 125

Ile Phe Leu Ile Asn Lys Pro Asp Gly Lys Lys Val Ala Val Leu Leu
130 135 140

Met Asp Thr Gln Gly Thr Phe Asp Ser Gln Ser Thr Leu Arg Asp Ser
145 150 155 160

Ala Thr Val Phe Ala Leu Ser Thr Met Ile Ser Ser Ile Gln Val Tyr
165 170 175

Asn Leu Ser Gln Asn Val Gln Glu Asp Asp Leu Gln His Leu Gln Leu
180 185 190

Phe Thr Glu Tyr Gly Arg Leu Ala Met Glu Glu Thr Phe Leu Lys Pro
195 200 205

Phe Gln Ser Leu Ile Phe Leu Val Arg Asp Trp Ser Phe Pro Tyr Glu
210 215 220

Phe Ser Tyr Gly Ala Asp Gly Gly Ala Lys Phe Leu Glu Lys Arg Leu
225 230 235 240

Lys Val Ser Gly Asn Gln His Glu Glu Leu Gln Asn Val Arg Lys His
245 250 255

Ile His Ser Cys Phe Thr Asn Ile Ser Cys Phe Leu Leu Pro His Pro
260 265 270

Gly Leu Lys Val Ala Thr Asn Pro Asn Phe Asp Gly Lys Leu Lys Glu
275 280 285

Ile Asp Asp Glu Phe Ile Lys Asn Leu Lys Ile Leu Ile Pro Trp Leu
290 295 300

Leu Ser Pro Glu Ser Leu Asp Ile Lys Glu Ile Asn Gly Asn Lys Ile
305 310 315 320

Thr Cys Arg Gly Leu Val Glu Tyr Phe Lys Ala Tyr Ile Lys Ile Tyr
325 330 335

Gln Gly Glu Glu Leu Pro His Pro Lys Ser Met Leu Gln Ala Thr Ala
340 345 350

Protein Complexes associated with APP-processing

Glu Ala Asn Asn Leu Ala Ala Val Ala Thr Ala Lys Asp Thr Tyr Asn
 355 360 365

Lys Lys Met Glu Glu Ile Cys Gly Gly Asp Lys Pro Phe Leu Ala Pro
 370 375 380

Asn Asp Leu Gln Thr Lys His Leu Gln Leu Lys Glu Glu Ser Val Lys
 385 390 395 400

Leu Phe Arg Gly Val Lys Lys Met Gly Gly Glu Glu Phe Ser Arg Arg
 405 410 415

Tyr Leu Gln Gln Leu Glu Ser Glu Ile Asp Glu Leu Tyr Ile Gln Tyr
 420 425 430

Ile Lys His Asn Asp Ser Lys Asn Ile Phe His Ala Ala Arg Thr Pro
 435 440 445

Ala Thr Leu Phe Val Val Ile Phe Ile Thr Tyr Val Ile Ala Gly Val
 450 455 460

Thr Gly Phe Ile Gly Leu Asp Ile Ile Ala Ser Leu Cys Asn Met Ile
 465 470 475 480

Met Gly Leu Thr Leu Ile Thr Leu Cys Thr Trp Ala Tyr Ile Arg Tyr
 485 490 495

Ser Gly Glu Tyr Arg Glu Leu Gly Ala Val Ile Asp Gln Val Ala Ala
 500 505 510

Ala Leu Trp Asp Gln Gly Ser Thr Asn Glu Ala Leu Tyr Lys Leu Tyr
 515 520 525

Ser Ala Ala Ala Thr His Arg His Leu Tyr His Gln Ala Phe Pro Thr
 530 535 540

Pro Lys Ser Glu Ser Thr Glu Gln Ser Glu Lys Lys Lys Met
 545 550 555

<210> 188

<211> 186

<212> PRT

<213> Homo sapiens

<400> 188

Val Gly Ser Leu Asn Cys Ile Val Ala Val Ser Gln Asn Met Gly Ile
 1 5 10 15

Protein Complexes associated with APP-processing
 Gly Lys Asn Gly Asp Leu Pro Trp Pro Pro Leu Arg Asn Glu Phe Arg
 20 25 30

Tyr Phe Gln Arg Met Thr Thr Thr Ser Ser Val Glu Gly Lys Gln Asn
 35 40 45

Leu Val Ile Met Gly Lys Lys Thr Trp Phe Ser Ile Pro Glu Lys Asn
 50 55 60

Arg Pro Leu Lys Gly Arg Ile Asn Leu Val Leu Ser Arg Glu Leu Lys
 65 70 75 80

Glu Pro Pro Gln Gly Ala His Phe Leu Ser Arg Ser Leu Asp Asp Ala
 85 90 95

Leu Lys Leu Thr Glu Gln Pro Glu Leu Ala Asn Lys Val Asp Met Val
 100 105 110

Trp Ile Val Gly Gly Ser Ser Val Tyr Lys Glu Ala Met Asn His Pro
 115 120 125

Gly His Leu Lys Leu Phe Val Thr Arg Ile Met Gln Asp Phe Glu Ser
 130 135 140

Asp Thr Phe Phe Pro Glu Ile Asp Leu Glu Lys Tyr Lys Leu Leu Pro
 145 150 155 160

Glu Tyr Pro Gly Val Leu Ser Asp Val Gln Glu Glu Lys Gly Ile Lys
 165 170 175

Tyr Lys Phe Glu Val Tyr Glu Lys Asn Asp
 180 185

<210> 189

<211> 1479

<212> PRT

<213> Homo sapiens

<400> 189

Met Gly Pro Gly Arg Pro Ala Pro Ala Pro Trp Pro Arg His Leu Leu
 1 5 10 15

Arg Cys Val Leu Leu Leu Gly Cys Leu His Leu Gly Arg Pro Gly Ala
 20 25 30

Pro Gly Asp Ala Ala Leu Pro Glu Pro Asn Val Phe Leu Ile Phe Ser
 35 40 45

Protein Complexes associated with APP-processing
 His Gly Leu Gln Gly Cys Leu Glu Ala Gln Gly Gly Gln Val Arg Val
 50 55 60

Thr Pro Ala Cys Asn Thr Ser Leu Pro Ala Gln Arg Trp Lys Trp Val
 65 70 75 80

Ser Arg Asn Arg Leu Phe Asn Leu Gly Thr Met Gln Cys Leu Gly Thr
 85 90 95

Gly Trp Pro Gly Thr Asn Thr Thr Ala Ser Leu Gly Met Tyr Glu Cys
 100 105 110

Asp Arg Glu Ala Leu Asn Leu Arg Trp His Cys Arg Thr Leu Gly Asp
 115 120 125

Gln Leu Ser Leu Leu Leu Gly Ala Arg Thr Ser Asn Ile Ser Lys Pro
 130 135 140

Gly Thr Leu Glu Arg Gly Asp Gln Thr Arg Ser Gly Gln Trp Arg Ile
 145 150 155 160

Tyr Gly Ser Glu Glu Asp Leu Cys Ala Leu Pro Tyr His Glu Val Tyr
 165 170 175

Thr Ile Gln Gly Asn Ser His Gly Lys Pro Cys Thr Ile Pro Phe Lys
 180 185 190

Tyr Asp Asn Gln Trp Phe His Gly Cys Thr Ser Thr Gly Arg Glu Asp
 195 200 205

Gly His Leu Trp Cys Ala Thr Thr Gln Asp Tyr Gly Lys Asp Glu Arg
 210 215 220

Trp Gly Phe Cys Pro Ile Lys Ser Asn Asp Cys Glu Thr Phe Trp Asp
 225 230 235 240

Lys Asp Gln Leu Thr Asp Ser Cys Tyr Gln Phe Asn Phe Gln Ser Thr
 245 250 255

Leu Ser Trp Arg Glu Ala Trp Ala Ser Cys Glu Gln Gln Gly Ala Asp
 260 265 270

Leu Leu Ser Ile Thr Glu Ile His Glu Gln Thr Tyr Ile Asn Gly Leu
 275 280 285

Leu Thr Gly Tyr Ser Ser Thr Leu Trp Ile Gly Leu Asn Asp Leu Asp
 290 295 300

Thr Ser Gly Gly Trp Gln Trp Ser Asp Asn Ser Pro Leu Lys Tyr Leu
 305 310 315 320

Protein Complexes associated with APP-processing

Asn Trp Glu Ser Asp Gln Pro Asp Asn Pro Ser Glu Glu Asn Cys Gly
 325 330 335

Val Ile Arg Thr Glu Ser Ser Gly Gly Trp Gln Asn Arg Asp Cys Ser
 340 345 350

Ile Ala Leu Pro Tyr Val Cys Lys Lys Lys Pro Asn Ala Thr Ala Glu
 355 360 365

Pro Thr Pro Pro Asp Arg Trp Ala Asn Val Lys Val Glu Cys Glu Pro
 370 375 380

Ser Trp Gln Pro Phe Gln Gly His Cys Tyr Arg Leu Gln Ala Glu Lys
 385 390 395 400

Arg Ser Trp Gln Glu Ser Lys Lys Ala Cys Leu Arg Gly Gly Gly Asp
 405 410 415

Leu Val Ser Ile His Ser Met Ala Glu Leu Glu Phe Ile Thr Lys Gln
 420 425 430

Ile Lys Gln Glu Val Glu Glu Leu Trp Ile Gly Leu Asn Asp Leu Lys
 435 440 445

Leu Gln Met Asn Phe Glu Trp Ser Asp Gly Ser Leu Val Ser Phe Thr
 450 455 460

His Trp His Pro Phe Glu Pro Asn Asn Phe Arg Asp Ser Leu Glu Asp
 465 470 475 480

Cys Val Thr Ile Trp Gly Pro Glu Gly Arg Trp Asn Asp Ser Pro Cys
 485 490 495

Asn Gln Ser Leu Pro Ser Ile Cys Lys Lys Ala Gly Gln Leu Ser Gln
 500 505 510

Gly Ala Ala Glu Glu Asp His Gly Cys Arg Lys Gly Trp Thr Trp His
 515 520 525

Ser Pro Ser Cys Tyr Trp Leu Gly Glu Asp Gln Val Thr Tyr Ser Glu
 530 535 540

Ala Arg Arg Leu Cys Thr Asp His Gly Ser Gln Leu Val Thr Ile Thr
 545 550 555 560

Asn Arg Phe Glu Gln Ala Phe Val Ser Ser Leu Ile Tyr Asn Trp Glu
 565 570 575

Gly Glu Tyr Phe Trp Thr Ala Leu Gln Asp Leu Asn Ser Thr Gly Ser
 580 585 590

Protein Complexes associated with APP-processing

Phe Phe Trp Leu Ser Gly Asp Glu Val Met Tyr Thr His Trp Asn Arg
595 600 605

Asp Gln Pro Gly Tyr Ser Arg Gly Gly Cys Val Ala Leu Ala Thr Gly
610 615 620

Ser Ala Met Gly Leu Trp Glu Val Lys Asn Cys Thr Ser Phe Arg Ala
625 630 635 640

Arg Tyr Ile Cys Arg Gln Ser Leu Gly Thr Pro Val Thr Pro Glu Leu
645 650 655

Pro Gly Pro Asp Pro Thr Pro Ser Leu Thr Gly Ser Cys Pro Gln Gly
660 665 670

Trp Ala Ser Asp Thr Lys Leu Arg Tyr Cys Tyr Lys Val Phe Ser Ser
675 680 685

Glu Arg Leu Gln Asp Lys Lys Ser Trp Val Gln Ala Gln Gly Ala Cys
690 695 700

Gln Glu Leu Gly Ala Gln Leu Leu Ser Leu Ala Ser Tyr Glu Glu Glu
705 710 715 720

His Phe Val Ala Asn Met Leu Asn Lys Ile Phe Gly Glu Ser Glu Pro
725 730 735

Glu Ile His Glu Gln His Trp Phe Trp Ile Gly Leu Asn Arg Arg Asp
740 745 750

Pro Arg Gly Gly Gln Ser Trp Arg Trp Ser Asp Gly Val Gly Phe Ser
755 760 765

Tyr His Asn Phe Asp Arg Ser Arg His Asp Asp Asp Ile Arg Gly
770 775 780

Cys Ala Val Leu Asp Leu Ala Ser Leu Gln Trp Val Ala Met Gln Cys
785 790 795 800

Asp Thr Gln Leu Asp Trp Ile Cys Lys Ile Pro Arg Gly Thr Asp Val
805 810 815

Arg Glu Pro Asp Asp Ser Pro Gln Gly Arg Arg Glu Trp Leu Arg Phe
820 825 830

Gln Glu Ala Glu Tyr Lys Phe Phe Glu His His Ser Thr Trp Ala Gln
835 840 845

Ala Gln Arg Ile Cys Thr Trp Phe Gln Ala Glu Leu Thr Ser Val His
850 855 860

Protein Complexes associated with APP-processing
 Ser Gln Ala Glu Leu Asp Phe Leu Ser His Asn Leu Gln Lys Phe Ser
 865 870 875 880

Arg Ala Gln Glu Gln His Trp Trp Ile Gly Leu His Thr Ser Glu Ser
 885 890 895

Asp Gly Arg Phe Arg Trp Thr Asp Gly Ser Ile Ile Asn Phe Ile Ser
 900 905 910

Trp Ala Pro Gly Lys Pro Arg Pro Val Gly Lys Asp Lys Lys Cys Val
 915 920 925

Tyr Met Thr Ala Ser Arg Glu Asp Trp Gly Asp Gln Arg Cys Leu Thr
 930 935 940

Ala Leu Pro Tyr Ile Cys Lys Arg Ser Asn Val Thr Lys Glu Thr Gln
 945 950 955 960

Pro Pro Asp Leu Pro Thr Thr Ala Leu Gly Gly Cys Pro Ser Asp Trp
 965 970 975

Ile Gln Phe Leu Asn Lys Cys Phe Gln Val Gln Gly Gln Glu Pro Gln
 980 985 990

Ser Arg Val Lys Trp Ser Glu Ala Gln Phe Ser Cys Glu Gln Gln Glu
 995 1000 1005

Ala Gln Leu Val Thr Ile Thr Asn Pro Leu Glu Gln Ala Phe Ile
 1010 1015 1020

Thr Ala Ser Leu Pro Asn Val Thr Phe Asp Leu Trp Ile Gly Leu
 1025 1030 1035

His Ala Ser Gln Arg Asp Phe Gln Trp Val Glu Gln Glu Pro Leu
 1040 1045 1050

Met Tyr Ala Asn Trp Ala Pro Gly Glu Pro Ser Gly Pro Ser Pro
 1055 1060 1065

Ala Pro Ser Gly Asn Lys Pro Thr Ser Cys Ala Val Val Leu His
 1070 1075 1080

Ser Pro Ser Ala His Phe Thr Gly Arg Trp Asp Asp Arg Ser Cys
 1085 1090 1095

Thr Glu Glu Thr His Gly Phe Ile Cys Gln Lys Gly Thr Asp Pro
 1100 1105 1110

Ser Leu Ser Pro Ser Pro Ala Ala Leu Pro Pro Ala Pro Gly Thr
 1115 1120 1125

Protein Complexes associated with APP-processing

Glu	Leu	Ser	Tyr	Leu	Asn	Gly	Thr	Phe	Arg	Leu	Leu	Gln	Lys	Pro
1130						1135						1140		
Leu	Arg	Trp	His	Asp	Ala	Leu	Leu	Leu	Cys	Glu	Ser	His	Asn	Ala
1145						1150					1155			
Ser	Leu	Ala	Tyr	Val	Pro	Asp	Pro	Tyr	Thr	Gln	Ala	Phe	Leu	Thr
1160						1165					1170			
Gln	Ala	Ala	Arg	Gly	Leu	Arg	Thr	Pro	Leu	Trp	Ile	Gly	Leu	Ala
1175						1180					1185			
Gly	Glu	Glu	Gly	Ser	Arg	Arg	Tyr	Ser	Trp	Val	Ser	Glu	Glu	Pro
1190						1195					1200			
Leu	Asn	Tyr	Val	Gly	Trp	Gln	Asp	Gly	Glu	Pro	Gln	Gln	Pro	Gly
1205						1210					1215			
Gly	Cys	Thr	Tyr	Val	Asp	Val	Asp	Gly	Ala	Trp	Arg	Thr	Thr	Ser
1220						1225					1230			
Cys	Asp	Thr	Lys	Leu	Gln	Gly	Ala	Val	Cys	Gly	Val	Ser	Ser	Gly
1235						1240					1245			
Pro	Pro	Pro	Pro	Arg	Arg	Ile	Ser	Tyr	His	Gly	Ser	Cys	Pro	Gln
1250						1255					1260			
Gly	Leu	Ala	Asp	Ser	Ala	Trp	Ile	Pro	Phe	Arg	Glu	His	Cys	Tyr
1265						1270					1275			
Ser	Phe	His	Met	Glu	Leu	Leu	Leu	Gly	His	Lys	Glu	Ala	Arg	Gln
1280						1285					1290			
Arg	Cys	Gln	Arg	Ala	Gly	Gly	Ala	Val	Leu	Ser	Ile	Leu	Asp	Glu
1295						1300					1305			
Met	Glu	Asn	Val	Phe	Val	Trp	Glu	His	Leu	Gln	Ser	Tyr	Glu	Gly
1310						1315					1320			
Gln	Ser	Arg	Gly	Ala	Trp	Leu	Gly	Met	Asn	Phe	Asn	Pro	Lys	Gly
1325						1330					1335			
Gly	Thr	Leu	Val	Trp	Gln	Asp	Asn	Thr	Ala	Val	Asn	Tyr	Ser	Asn
1340						1345					1350			
Trp	Gly	Pro	Pro	Gly	Leu	Gly	Pro	Ser	Met	Leu	Ser	His	Asn	Ser
1355						1360					1365			
Cys	Tyr	Trp	Ile	Gln	Ser	Asn	Ser	Gly	Leu	Trp	Arg	Pro	Gly	Ala
1370						1375					1380			

Protein Complexes associated with APP-processing
 Cys Thr Asn Ile Thr Met Gly Val Val Cys Lys Leu Pro Arg Ala
 1385 1390 1395

Glu Gln Ser Ser Phe Ser Pro Ser Ala Leu Pro Glu Asn Pro Ala
 1400 1405 1410

Ala Leu Val Val Val Leu Met Ala Val Leu Leu Leu Leu Ala Leu
 1415 1420 1425

Leu Thr Ala Ala Leu Ile Leu Tyr Arg Arg Arg Gln Ser Ile Glu
 1430 1435 1440

Arg Gly Ala Phe Glu Gly Ala Arg Tyr Ser Arg Ser Ser Ser Ser
 1445 1450 1455

Pro Thr Glu Ala Thr Glu Lys Asn Ile Leu Val Ser Asp Met Glu
 1460 1465 1470

Met Asn Glu Gln Gln Glu
 1475

<210> 190

<211> 506

<212> PRT

<213> Homo sapiens

<400> 190

Met Glu Asp His Gln His Val Pro Ile Asp Ile Gln Thr Ser Lys Leu
 1 5 10 15

Leu Asp Trp Leu Val Asp Arg Arg His Cys Ser Leu Lys Trp Gln Ser
 20 25 30

Leu Val Leu Thr Ile Arg Glu Lys Ile Asn Ala Ala Ile Gln Asp Met
 35 40 45

Pro Glu Ser Glu Glu Ile Ala Gln Leu Leu Ser Gly Ser Tyr Ile His
 50 55 60

Tyr Phe His Cys Leu Arg Ile Leu Asp Leu Leu Lys Gly Thr Glu Ala
 65 70 75 80

Ser Thr Lys Asn Ile Phe Gly Arg Tyr Ser Ser Gln Arg Met Lys Asp
 85 90 95

Trp Gln Glu Ile Ile Ala Leu Tyr Glu Lys Asp Asn Thr Tyr Leu Val
 100 105 110

Protein Complexes associated with APP-processing

Glu Leu Ser Ser Leu Leu Val Arg Asn Val Asn Tyr Glu Ile Pro Ser
 115 120 125

Leu Lys Lys Gln Ile Ala Lys Cys Gln Gln Leu Gln Gln Glu Tyr Ser
 130 135 140

Arg Lys Glu Glu Glu Cys Gln Ala Gly Ala Ala Glu Met Arg Glu Gln
 145 150 155 160

Phe Tyr His Ser Cys Lys Gln Tyr Gly Ile Thr Gly Glu Asn Val Arg
 165 170 175

Gly Glu Leu Leu Ala Leu Val Lys Asp Leu Pro Ser Gln Leu Ala Glu
 180 185 190

Ile Gly Ala Ala Ala Gln Gln Ser Leu Gly Glu Ala Ile Asp Val Tyr
 195 200 205

Gln Ala Ser Val Gly Phe Val Cys Glu Ser Pro Thr Glu Gln Val Leu
 210 215 220

Pro Met Leu Arg Phe Val Gln Lys Arg Gly Asn Ser Thr Val Tyr Glu
 225 230 235 240

Trp Arg Thr Gly Thr Glu Pro Ser Val Val Glu Arg Pro His Leu Glu
 245 250 255

Glu Leu Pro Glu Gln Val Ala Glu Asp Ala Ile Asp Trp Gly Asp Phe
 260 265 270

Gly Val Glu Ala Val Ser Glu Gly Thr Asp Ser Gly Ile Ser Ala Glu
 275 280 285

Ala Ala Gly Ile Asp Trp Gly Ile Phe Pro Glu Ser Asp Ser Lys Asp
 290 295 300

Pro Gly Gly Asp Gly Ile Asp Trp Gly Asp Asp Ala Val Ala Leu Gln
 305 310 315 320

Ile Thr Val Leu Glu Ala Gly Thr Gln Ala Pro Glu Gly Val Ala Arg
 325 330 335

Gly Pro Asp Ala Leu Thr Leu Leu Glu Tyr Thr Glu Thr Arg Asn Gln
 340 345 350

Phe Leu Asp Glu Leu Met Glu Leu Glu Ile Phe Leu Ala Gln Arg Ala
 355 360 365

Val Glu Leu Ser Glu Glu Ala Asp Val Leu Ser Val Ser Gln Phe Gln
 370 375 380

Protein Complexes associated with APP-processing
 Leu Ala Pro Ala Ile Leu Gln Gly Gln Thr Lys Glu Lys Met Val Thr
 385 390 395 400

Met Val Ser Val Leu Glu Asp Leu Ile Gly Lys Leu Thr Ser Leu Gln
 405 410 415

Leu Gln His Leu Phe Met Ile Leu Ala Ser Pro Arg Tyr Val Asp Arg
 420 425 430

Val Thr Glu Phe Leu Gln Gln Lys Leu Lys Gln Ser Gln Leu Leu Ala
 435 440 445

Leu Lys Lys Glu Leu Met Val Gln Lys Gln Gln Glu Ala Leu Glu Glu
 450 455 460

Gln Ala Ala Leu Glu Pro Lys Leu Asp Leu Leu Leu Glu Lys Thr Lys
 465 470 475 480

Glu Leu Gln Lys Leu Ile Glu Ala Asp Ile Ser Lys Arg Tyr Ser Gly
 485 490 495

Arg Pro Val Asn Leu Met Gly Thr Ser Leu
 500 505

<210> 191

<211> 820

<212> PRT

<213> Homo sapiens

<400> 191

Gly Gly Arg Gln Arg Cys Gln Arg Gly Arg Ser Cys Gly Ala Arg Glu
 1 5 10 15

Glu Glu Val Glu Pro Gly Thr Ala Arg Pro Pro Pro Ala Ala Ser Ala
 20 25 30

Met Asp Ala Ser Leu Glu Lys Ile Ala Asp Pro Thr Leu Ala Glu Met
 35 40 45

Gly Lys Asn Leu Lys Glu Ala Val Lys Met Leu Glu Asp Ser Gln Arg
 50 55 60

Arg Thr Glu Glu Glu Asn Gly Lys Lys Leu Ile Ser Gly Asp Ile Pro
 65 70 75 80

Gly Pro Leu Gln Gly Ser Gly Gln Asp Met Val Ser Ile Leu Gln Leu
 85 90 95

Protein Complexes associated with APP-processing

Val Gln Asn Leu Met His Gly Asp Glu Asp Glu Glu Pro Gln Ser Pro
100 105 110

Arg Ile Gln Asn Ile Gly Glu Gln Gly His Met Ala Leu Leu Gly His
115 120 125

Ser Leu Gly Ala Tyr Ile Ser Thr Leu Asp Lys Glu Lys Leu Arg Lys
130 135 140

Leu Thr Thr Arg Ile Leu Ser Asp Thr Thr Leu Trp Leu Cys Arg Ile
145 150 155 160

Phe Arg Tyr Glu Asn Gly Cys Ala Tyr Phe His Glu Glu Glu Arg Glu
165 170 175

Gly Leu Ala Lys Ile Cys Arg Leu Ala Ile His Ser Arg Tyr Glu Asp
180 185 190

Phe Val Val Asp Gly Phe Asn Val Leu Tyr Asn Lys Lys Pro Val Ile
195 200 205

Tyr Leu Ser Ala Ala Ala Arg Pro Gly Leu Gly Gln Tyr Leu Cys Asn
210 215 220

Gln Leu Gly Leu Pro Phe Pro Cys Leu Cys Arg Val Pro Cys Asn Thr
225 230 235 240

Val Phe Gly Ser Gln His Gln Met Asp Val Ala Phe Leu Glu Lys Leu
245 250 255

Ile Lys Asp Asp Ile Glu Arg Gly Arg Leu Pro Leu Leu Leu Val Ala
260 265 270

Asn Ala Gly Thr Ala Ala Val Gly His Thr Asp Lys Ile Gly Arg Leu
275 280 285

Lys Glu Leu Cys Glu Gln Tyr Gly Ile Trp Leu His Val Glu Gly Val
290 295 300

Asn Leu Ala Thr Leu Ala Leu Gly Tyr Val Ser Ser Ser Val Leu Ala
305 310 315 320

Ala Ala Lys Cys Asp Ser Met Thr Met Thr Pro Gly Pro Trp Leu Gly
325 330 335

Leu Pro Ala Val Pro Ala Val Thr Leu Tyr Lys His Asp Asp Pro Ala
340 345 350

Leu Thr Leu Val Ala Gly Leu Thr Ser Asn Lys Pro Thr Asp Lys Leu
355 360 365

Protein Complexes associated with APP-processing

Arg Ala Leu Pro Leu Trp Leu Ser Leu Gln Tyr Leu Gly Leu Asp Gly
 370 375 380

Phe Val Glu Arg Ile Lys His Ala Cys Gln Leu Ser Gln Arg Leu Gln
 385 390 395 400

Glu Ser Leu Lys Lys Val Asn Tyr Ile Lys Ile Leu Val Glu Asp Glu
 405 410 415

Leu Ser Ser Pro Val Val Val Phe Arg Phe Phe Gln Glu Leu Pro Gly
 420 425 430

Ser Asp Pro Val Phe Lys Ala Val Pro Val Pro Asn Met Thr Pro Ser
 435 440 445

Gly Val Gly Arg Glu Arg His Ser Cys Asp Ala Leu Asn Arg Trp Leu
 450 455 460

Gly Glu Gln Leu Lys Gln Leu Val Pro Ala Ser Gly Leu Thr Val Met
 465 470 475 480

Asp Leu Glu Ala Glu Gly Thr Cys Leu Arg Phe Ser Pro Leu Met Thr
 485 490 495

Ala Ala Val Leu Gly Thr Arg Gly Glu Asp Val Asp Gln Leu Val Ala
 500 505 510

Cys Ile Glu Ser Lys Leu Pro Val Leu Cys Cys Thr Leu Gln Leu Arg
 515 520 525

Glu Glu Phe Lys Gln Glu Val Glu Ala Thr Ala Gly Leu Leu Tyr Val
 530 535 540

Asp Asp Pro Asn Trp Ser Gly Ile Gly Val Val Arg Tyr Glu His Ala
 545 550 555 560

Asn Asp Asp Lys Ser Ser Leu Lys Ser Asp Pro Glu Gly Glu Asn Ile
 565 570 575

His Ala Gly Leu Leu Lys Lys Leu Asn Glu Leu Glu Ser Asp Leu Thr
 580 585 590

Phe Lys Ile Gly Pro Glu Tyr Lys Ser Met Lys Ser Cys Leu Tyr Val
 595 600 605

Gly Met Ala Ser Asp Asn Val Asp Ala Ala Glu Leu Val Glu Thr Ile
 610 615 620

Ala Ala Thr Ala Arg Glu Ile Glu Glu Asn Ser Arg Leu Leu Glu Asn
 625 630 635 640

Protein Complexes associated with APP-processing
 Met Thr Glu Val Val Arg Lys Gly Ile Gln Glu Ala Gln Val Glu Leu
 645 650 655

Gln Lys Ala Ser Glu Glu Arg Leu Leu Glu Glu Gly Val Leu Arg Gln
 660 665 670

Ile Pro Val Val Gly Ser Val Leu Asn Trp Phe Ser Pro Val Gln Ala
 675 680 685

Leu Gln Lys Gly Arg Thr Phe Asn Leu Thr Ala Gly Ser Leu Glu Ser
 690 695 700

Thr Glu Pro Ile Tyr Val Tyr Lys Ala Gln Gly Ala Gly Val Thr Leu
 705 710 715 720

Pro Pro Thr Pro Ser Gly Ser Arg Thr Lys Gln Arg Leu Pro Gly Gln
 725 730 735

Lys Pro Phe Lys Arg Ser Leu Arg Gly Ser Asp Ala Leu Ser Glu Thr
 740 745 750

Ser Ser Val Ser His Ile Glu Asp Leu Glu Lys Val Glu Arg Leu Ser
 755 760 765

Ser Gly Pro Glu Gln Ile Thr Leu Glu Ala Ser Ser Thr Glu Gly His
 770 775 780

Pro Gly Ala Pro Ser Pro Gln His Thr Asp Gln Thr Glu Ala Phe Gln
 785 790 795 800

Lys Gly Val Pro His Pro Glu Asp Asp His Ser Gln Val Glu Gly Pro
 805 810 815

Glu Ser Leu Arg
 820

<210> 192

<211> 1522

<212> PRT

<213> Homo sapiens

<400> 192

Glu Pro Cys Ala Leu Thr Pro Gly Pro Ser His Leu Ala Leu Thr Phe
 1 5 10 15

Leu Pro Ser Lys Pro Gly Ala Arg Pro Gln Pro Glu Gly Ala Ser Trp
 20 25 30

Protein Complexes associated with APP-processing

Asp Ala Gly Pro Gly Gly Ala Pro Ser Ala Trp Ala Asp Pro Gly Glu
 35 40 45

Gly Gly Pro Ser Pro Met Leu Leu Pro Glu Gly Leu Ser Ser Gln Ala
 50 55 60

Leu Ser Thr Glu Ala Pro Leu Pro Ala Thr Leu Glu Pro Arg Ile Val
 65 70 75 80

Met Gly Glu Glu Thr Cys Gln Ala Leu Leu Ser Pro Arg Ala Ala Arg
 85 90 95

Thr Ala Leu Arg Asp Gln Glu Gly Gly His Ala Ser Pro Asp Pro Pro
 100 105 110

Pro Glu Leu Cys Ser Gln Gly Asp Leu Ser Val Pro Ser Pro Pro Pro
 115 120 125

Asp Pro Asp Ser Phe Phe Thr Pro Pro Ser Thr Pro Thr Lys Thr Thr
 130 135 140

Tyr Ala Leu Leu Pro Ala Cys Gly Pro His Gly Asp Ala Arg Asp Ser
 145 150 155 160

Glu Ala Glu Leu Arg Asp Glu Leu Leu Asp Ser Pro Pro Ala Ser Pro
 165 170 175

Ser Gly Ser Tyr Ile Thr Ala Asp Gly Asp Ser Trp Ala Ser Ser Pro
 180 185 190

Ser Cys Ser Leu Ser Leu Leu Ala Pro Ala Glu Gly Leu Asp Phe Pro
 195 200 205

Ser Gly Trp Gly Leu Ser Pro Gln Gly Ser Met Val Asp Glu Arg Glu
 210 215 220

Leu His Pro Ala Gly Thr Pro Glu Pro Pro Ser Ser Glu Ser Ser Leu
 225 230 235 240

Ser Ala Asp Ser Ser Ser Ser Trp Gly Gln Glu Gly His Phe Phe Asp
 245 250 255

Leu Asp Phe Leu Ala Asn Asp Pro Met Ile Pro Ala Ala Leu Leu Pro
 260 265 270

Phe Gln Gly Ser Leu Ile Phe Gln Val Glu Ala Val Glu Val Thr Pro
 275 280 285

Leu Ser Pro Glu Glu Glu Glu Glu Glu Ala Val Ala Asp Pro Asp Pro
 290 295 300

Protein Complexes associated with APP-processing

Gly Gly Asp Leu Ala Gly Glu Gly Glu Glu Asp Ser Thr Ser Ala Ser
 305 310 315 320

Phe Leu Gln Ser Leu Ser Asp Leu Ser Ile Thr Glu Gly Met Asp Glu
 325 330 335

Ala Phe Ala Phe Arg Asp Asp Thr Ser Ala Ala Ser Ser Asp Ser Asp
 340 345 350

Ser Ala Ser Tyr Ala Glu Ala Asp Asp Glu Arg Leu Tyr Ser Gly Glu
 355 360 365

Pro His Ala Gln Ala Thr Leu Leu Gln Asp Ser Val Gln Lys Thr Glu
 370 375 380

Glu Glu Ser Gly Gly Gly Ala Lys Gly Leu Gln Ala Gln Asp Gly Thr
 385 390 395 400

Val Ser Trp Ala Val Glu Ala Ala Pro Gln Thr Ser Asp Arg Gly Ala
 405 410 415

Tyr Leu Ser Gln Arg Gln Glu Leu Ile Ser Glu Val Thr Glu Glu Gly
 420 425 430

Leu Ala Leu Gly Gln Glu Ser Thr Ala Thr Val Thr Pro His Thr Leu
 435 440 445

Gln Val Ala Pro Gly Leu Gln Val Glu Val Ala Thr Arg Val Thr Pro
 450 455 460

Gln Ala Gly Glu Glu Glu Thr Asp Ser Thr Ala Gly Gln Glu Ser Ala
 465 470 475 480

Ala Met Ala Met Pro Gln Pro Ser Gln Glu Gly Ile Ser Glu Ile Leu
 485 490 495

Gly Gln Glu Ser Val Thr Ala Glu Lys Leu Pro Thr Pro Gln Glu Glu
 500 505 510

Thr Ser Leu Thr Leu Cys Pro Asp Ser Pro Gln Asn Leu Lys Glu Glu
 515 520 525

Gly Gly Leu Asp Leu Pro Ser Gly Arg Lys Pro Val Ala Ala Ala Thr
 530 535 540

Ile Val Pro Arg Gln Ala Lys Glu Asp Leu Thr Leu Pro Gln Asp Ser
 545 550 555 560

Ala Met Thr Pro Pro Leu Pro Leu Gln Asp Thr Asp Leu Ser Ser Ala
 565 570 575

Protein Complexes associated with APP-processing

Pro Lys Pro Val Ala Ala Ala Thr Ile Val Ser Gln Gln Ala Glu Glu
580 585 590

Gly Leu Thr Leu Pro Gln Asp Ser Val Met Thr Pro Pro Leu Pro Leu
595 600 605

Gln Asp Thr Glu Leu Ser Ser Ala Pro Lys Pro Val Ala Ala Ala Thr
610 615 620

Leu Val Ser Gln Gln Ala Glu Glu Gly Leu Thr Leu Pro Gln Asp Ser
625 630 635 640

Ala Met Thr Pro Pro Leu Pro Leu Gln Asp Thr Asp Leu Ser Ser Ala
645 650 655

Pro Lys Pro Val Ala Ala Ala Thr Leu Val Ser Gln Gln Ala Glu Glu
660 665 670

Gly Leu Thr Leu Pro Gln Asp Ser Ala Met Thr Pro Pro Leu Pro Leu
675 680 685

Gln Asp Thr Asp Leu Ser Ser Ala Pro Lys Pro Val Ala Ala Ala Thr
690 695 700

Leu Val Ser Gln Gln Ala Glu Glu Gly Leu Thr Leu Pro Gln Asp Ser
705 710 715 720

Ala Met Thr Pro Pro Leu Pro Leu Gln Asp Thr Asp Leu Ser Ser Ala
725 730 735

Pro Lys Pro Val Ala Ala Ala Thr Ile Val Ser Gln Gln Ala Glu Glu
740 745 750

Gly Leu Thr Leu Pro Gln Asp Ser Ala Met Thr Pro Pro Leu Pro Leu
755 760 765

Gln Asp Thr Asp Leu Ser Ser Ala Pro Lys Pro Val Ala Ala Ala Thr
770 775 780

Ile Val Ser Gln Gln Ala Glu Glu Gly Leu Thr Leu Pro Gln Asp Ser
785 790 795 800

Ala Met Thr Pro Pro Leu Pro Leu Gln Asp Thr Asp Leu Ser Ser Ala
805 810 815

Pro Lys Pro Val Ala Ala Ala Thr Pro Val Ser Gln Gln Ala Glu Glu
820 825 830

Gly Leu Thr Leu Pro Gln Asp Ser Ala Met Thr Pro Pro Leu Pro Leu
835 840 845

Protein Complexes associated with APP-processing

Gln Asp Thr Asp Leu Ser Ser Ala Pro Lys Pro Val Ala Ala Ala Thr
 850 855 860

Pro Val Ser Gln Gln Ala Glu Glu Gly Leu Thr Leu Pro Gln Asp Ser
 865 870 875 880

Ala Met Thr Ala Pro Leu Pro Leu Gln Asp Thr Gly Pro Thr Ser Gly
 885 890 895

Pro Glu Pro Leu Ala Val Ala Thr Pro Gln Thr Leu Gln Ala Glu Ala
 900 905 910

Gly Cys Ala Pro Gly Thr Glu Pro Val Ala Thr Met Ala Gln Gln Glu
 915 920 925

Val Gly Glu Ala Leu Gly Pro Arg Pro Ala Pro Glu Glu Lys Asn Ala
 930 935 940

Ala Leu Pro Thr Val Pro Glu Pro Ala Ala Leu Asp Gln Val Gln Gln
 945 950 955 960

Asp Asp Pro Gln Pro Ala Ala Glu Ala Gly Thr Pro Trp Ala Ala Gln
 965 970 975

Glu Asp Ala Asp Ser Thr Leu Gly Met Glu Ala Leu Ser Leu Pro Glu
 980 985 990

Pro Ala Ser Gly Ala Gly Glu Glu Ile Ala Glu Ala Leu Ser Arg Pro
 995 1000 1005

Gly Arg Glu Ala Cys Leu Glu Ala Arg Ala His Thr Gly Asp Gly
 1010 1015 1020

Ala Lys Pro Asp Ser Pro Gln Lys Glu Thr Leu Glu Val Glu Asn
 1025 1030 1035

Gln Gln Glu Gly Gly Leu Lys Leu Leu Ala Gln Glu His Gly Pro
 1040 1045 1050

Arg Ser Ala Leu Gly Gly Ala Arg Glu Val Pro Asp Ala Pro Pro
 1055 1060 1065

Ala Ala Cys Pro Glu Val Ser Gln Ala Arg Leu Leu Ser Pro Ala
 1070 1075 1080

Arg Glu Glu Arg Gly Leu Ser Gly Lys Ser Thr Pro Glu Pro Thr
 1085 1090 1095

Leu Pro Ser Ala Val Ala Thr Glu Ala Ser Leu Asp Ser Cys Pro
 1100 1105 1110

Protein Complexes associated with APP-processing

Glu	Ser	Ser	Val	Gly	Ala	Val	Ser	Ser	Leu	Asp	Arg	Gly	Cys	Pro
	1115					1120					1125			
Asp	Ala	Pro	Ala	Pro	Thr	Ser	Ala	Pro	Thr	Ser	Gln	Gln	Pro	Glu
	1130					1135					1140			
Pro	Val	Leu	Gly	Leu	Gly	Ser	Val	Glu	Gln	Pro	His	Glu	Val	Pro
	1145					1150					1155			
Ser	Val	Leu	Gly	Thr	Pro	Leu	Leu	Gln	Pro	Pro	Glu	Asn	Leu	Ala
	1160					1165					1170			
Lys	Gly	Gln	Pro	Ser	Thr	Pro	Val	Asp	Arg	Pro	Leu	Gly	Pro	Asp
	1175					1180					1185			
Pro	Ser	Ala	Pro	Gly	Thr	Leu	Ala	Gly	Ala	Ala	Leu	Pro	Pro	Leu
	1190					1195					1200			
Glu	Pro	Pro	Ala	Pro	Cys	Leu	Cys	Gln	Asp	Pro	Gln	Glu	Asp	Ser
	1205					1210					1215			
Val	Glu	Asp	Glu	Glu	Pro	Pro	Gly	Ser	Leu	Gly	Leu	Pro	Pro	Pro
	1220					1225					1230			
Gln	Ala	Gly	Val	Gln	Pro	Ala	Ala	Ala	Ala	Val	Ser	Gly	Thr	Thr
	1235					1240					1245			
Gln	Pro	Leu	Gly	Thr	Gly	Pro	Arg	Val	Ser	Leu	Ser	Pro	His	Ser
	1250					1255					1260			
Pro	Leu	Leu	Ser	Pro	Lys	Val	Ala	Ser	Met	Asp	Ala	Lys	Asp	Leu
	1265					1270					1275			
Ala	Leu	Gln	Ile	Leu	Pro	Pro	Cys	Gln	Val	Pro	Pro	Pro	Ser	Gly
	1280					1285					1290			
Pro	Gln	Ser	Pro	Ala	Gly	Pro	Gln	Gly	Leu	Ser	Ala	Pro	Glu	Gln
	1295					1300					1305			
Gln	Glu	Asp	Glu	Asp	Ser	Leu	Glu	Glu	Asp	Ser	Pro	Arg	Ala	Leu
	1310					1315					1320			
Gly	Ser	Gly	Gln	His	Ser	Asp	Ser	His	Gly	Glu	Ser	Ser	Ala	Glu
	1325					1330					1335			
Leu	Asp	Glu	Gln	Asp	Ile	Leu	Ala	Pro	Gln	Thr	Val	Gln	Cys	Pro
	1340					1345					1350			
Ala	Gln	Ala	Pro	Ala	Gly	Gly	Ser	Glu	Glu	Thr	Ile	Ala	Lys	Ala
	1355					1360					1365			

Protein Complexes associated with APP-processing

Lys Gln Ser Arg Ser Glu Lys Lys Ala Arg Lys Ala Met Ser Lys
 1370 1375 1380

Leu Gly Leu Arg Gln Ile Gln Gly Val Thr Arg Ile Thr Ile Gln
 1385 1390 1395

Lys Ser Lys Asn Ile Leu Phe Val Ile Ala Lys Pro Asp Val Phe
 1400 1405 1410

Lys Ser Pro Ala Ser Asp Thr Tyr Val Val Phe Gly Glu Ala Lys
 1415 1420 1425

Ile Glu Asp Leu Ser Gln Gln Val His Lys Ala Ala Ala Glu Lys
 1430 1435 1440

Phe Lys Val Pro Ser Glu Pro Ser Ala Leu Val Pro Glu Ser Ala
 1445 1450 1455

Pro Arg Pro Arg Val Arg Leu Glu Cys Lys Glu Glu Glu Glu Glu
 1460 1465 1470

Glu Glu Glu Glu Val Asp Glu Ala Gly Leu Glu Leu Arg Asp Ile
 1475 1480 1485

Glu Leu Val Met Ala Gln Ala Asn Val Ser Arg Ala Lys Ala Val
 1490 1495 1500

Arg Ala Leu Arg Asp Asn His Ser Asp Ile Val Asn Ala Ile Met
 1505 1510 1515

Glu Leu Thr Met
 1520

<210> 193

<211> 648

<212> PRT

<213> Homo sapiens

<400> 193

Met Leu Thr Thr Leu Lys Pro Phe Gly Ser Val Ser Val Glu Ser Lys
 1 5 10 15

Met Asn Asn Lys Ala Gly Ser Phe Phe Trp Asn Leu Arg Gln Phe Ser
 20 25 30

Thr Leu Val Ser Thr Ser Arg Thr Met Arg Leu Cys Cys Leu Gly Leu
 35 40 45

Protein Complexes associated with APP-processing

Cys Lys Pro Lys Ile Val His Ser Asn Trp Asn Ile Leu Asn Asn Phe
 50 55 60

His Asn Arg Met Gln Ser Thr Asp Ile Ile Arg Tyr Leu Phe Gln Asp
 65 70 75 80

Ala Phe Ile Phe Lys Ser Asp Val Gly Phe Gln Thr Lys Gly Ile Ser
 85 90 95

Thr Leu Thr Ala Leu Arg Ile Glu Arg Leu Leu Tyr Ala Lys Arg Leu
 100 105 110

Phe Phe Asp Ser Lys Gln Ser Leu Val Pro Val Asp Lys Ser Asp Asp
 115 120 125

Glu Leu Lys Lys Val Asn Leu Asn His Glu Val Ser Asn Glu Asp Val
 130 135 140

Leu Thr Lys Glu Thr Lys Pro Asn Arg Ile Ser Ser Arg Lys Leu Ser
 145 150 155 160

Glu Glu Cys Asn Ser Leu Ser Asp Val Leu Asp Ala Phe Ser Lys Ala
 165 170 175

Pro Thr Phe Pro Ser Ser Asn Tyr Phe Thr Ala Met Trp Thr Ile Ala
 180 185 190

Lys Arg Leu Ser Asp Asp Gln Lys Arg Phe Glu Lys Arg Leu Met Phe
 195 200 205

Ser His Pro Ala Phe Asn Gln Leu Cys Glu His Met Met Arg Glu Ala
 210 215 220

Lys Ile Met Gln Tyr Lys Tyr Leu Leu Phe Ser Leu His Ala Ile Val
 225 230 235 240

Lys Leu Gly Ile Pro Gln Asn Thr Ile Leu Val Gln Thr Leu Leu Arg
 245 250 255

Val Thr Gln Glu Arg Ile Asn Glu Cys Asp Glu Ile Cys Leu Ser Val
 260 265 270

Leu Ser Thr Val Leu Glu Ala Met Glu Pro Cys Lys Asn Val His Val
 275 280 285

Leu Arg Thr Gly Phe Arg Ile Leu Val Asp Gln Gln Val Trp Lys Ile
 290 295 300

Glu Asp Val Phe Thr Leu Gln Val Val Met Lys Cys Ile Gly Lys Asp
 305 310 315 320

Protein Complexes associated with APP-processing

Ala Pro Ile Ala Leu Lys Arg Lys Leu Glu Met Lys Ala Leu Arg Glu
325 330 335

Leu Asp Arg Phe Ser Val Leu Asn Ser Gln His Met Phe Glu Val Leu
340 345 350

Ala Ala Met Asn His Arg Ser Leu Ile Leu Leu Asp Glu Cys Ser Lys
355 360 365

Val Val Leu Asp Asn Ile His Gly Cys Pro Leu Arg Ile Met Ile Asn
370 375 380

Ile Leu Gln Ser Cys Lys Asp Leu Gln Tyr His Asn Leu Asp Leu Phe
385 390 395 400

Lys Gly Leu Ala Asp Tyr Val Ala Ala Thr Phe Asp Ile Trp Lys Phe
405 410 415

Arg Lys Val Leu Phe Ile Leu Ile Leu Phe Glu Asn Leu Gly Phe Arg
420 425 430

Pro Val Gly Leu Met Asp Leu Phe Met Lys Arg Ile Val Glu Asp Pro
435 440 445

Glu Ser Leu Asn Met Lys Asn Ile Leu Ser Ile Leu His Thr Tyr Ser
450 455 460

Ser Leu Asn His Val Tyr Lys Cys Gln Asn Lys Glu Gln Phe Val Glu
465 470 475 480

Val Met Ala Ser Ala Leu Thr Gly Tyr Leu His Thr Ile Ser Ser Glu
485 490 495

Asn Leu Leu Asp Ala Val Tyr Ser Phe Cys Leu Met Asn Tyr Phe Pro
500 505 510

Leu Ala Pro Phe Asn Gln Leu Leu Gln Lys Asp Ile Ile Ser Glu Leu
515 520 525

Leu Thr Ser Asp Asp Met Lys Asn Ala Tyr Lys Leu His Thr Leu Asp
530 535 540

Thr Cys Leu Lys Leu Asp Asp Thr Val Tyr Leu Arg Asp Ile Ala Leu
545 550 555 560

Ser Leu Pro Gln Leu Pro Arg Glu Leu Pro Ser Ser His Thr Asn Ala
565 570 575

Lys Val Ala Glu Val Leu Ser Ser Leu Leu Gly Gly Glu Gly His Phe
580 585 590

Protein Complexes associated with APP-processing

Ser Lys Asp Val His Leu Pro His Asn Tyr His Ile Asp Phe Glu Ile
 595 600 605

Arg Met Asp Thr Asn Arg Asn Gln Val Leu Pro Leu Ser Asp Val Asp
 610 615 620

Thr Thr Ser Ala Thr Asp Ile Gln Arg Leu Leu Thr Tyr Ile Ser Phe
 625 630 635 640

Ala Gly Leu Ser Glu Leu Lys Ser
 645

<210> 194

<211> 1777

<212> PRT

<213> Homo sapiens

<400> 194

Leu Gln Leu Ser Val Lys Met Ser Val Leu Ile Ser Gln Ser Val Ile
 1 5 10 15

Asn Tyr Val Glu Glu Glu Asn Ile Pro Ala Leu Lys Ala Leu Leu Glu
 20 25 30

Lys Cys Lys Asp Val Asp Glu Arg Asn Glu Cys Gly Gln Thr Pro Leu
 35 40 45

Met Ile Ala Ala Glu Gln Gly Asn Leu Glu Ile Val Lys Glu Leu Ile
 50 55 60

Lys Asn Gly Ala Asn Cys Asn Leu Glu Asp Leu Asp Asn Trp Thr Ala
 65 70 75 80

Leu Ile Ser Ala Ser Lys Glu Gly His Val His Ile Val Glu Glu Leu
 85 90 95

Leu Lys Cys Gly Val Asn Leu Glu His Arg Asp Met Gly Gly Trp Thr
 100 105 110

Ala Leu Met Trp Ala Cys Tyr Lys Gly Arg Thr Asp Val Val Glu Leu
 115 120 125

Leu Leu Ser His Gly Ala Asn Pro Ser Val Thr Gly Leu Tyr Ser Val
 130 135 140

Tyr Pro Ile Ile Trp Ala Ala Gly Arg Gly His Ala Asp Ile Val His
 145 150 155 160

Protein Complexes associated with APP-processing

Leu Leu Leu Gln Asn Gly Ala Lys Val Asn Cys Ser Asp Lys Tyr Gly
 165 170 175

Thr Thr Pro Leu Val Trp Ala Ala Arg Lys Gly His Leu Glu Cys Val
 180 185 190

Lys His Leu Leu Ala Met Gly Ala Asp Val Asp Gln Glu Gly Ala Asn
 195 200 205

Ser Met Thr Ala Leu Ile Val Ala Val Lys Gly Gly Tyr Thr Gln Ser
 210 215 220

Val Lys Glu Ile Leu Lys Arg Asn Pro Asn Val Asn Leu Thr Asp Lys
 225 230 235 240

Asp Gly Asn Thr Ala Leu Met Ile Ala Ser Lys Glu Gly His Thr Glu
 245 250 255

Ile Val Gln Asp Leu Leu Asp Ala Gly Thr Tyr Val Asn Ile Pro Asp
 260 265 270

Arg Ser Gly Asp Thr Val Leu Ile Gly Ala Val Arg Gly Gly His Val
 275 280 285

Glu Ile Val Arg Ala Leu Leu Gln Lys Tyr Ala Asp Ile Asp Ile Arg
 290 295 300

Gly Gln Asp Asn Lys Thr Ala Leu Tyr Trp Ala Val Glu Lys Gly Asn
 305 310 315 320

Ala Thr Met Val Arg Asp Ile Leu Gln Cys Asn Pro Asp Thr Glu Ile
 325 330 335

Cys Thr Lys Asp Gly Glu Thr Pro Leu Ile Lys Ala Thr Lys Met Arg
 340 345 350

Asn Ile Glu Val Val Glu Leu Leu Leu Asp Lys Gly Ala Lys Val Ser
 355 360 365

Ala Val Asp Lys Lys Gly Asp Thr Pro Leu His Ile Ala Ile Arg Gly
 370 375 380

Arg Ser Arg Lys Leu Ala Glu Leu Leu Leu Arg Asn Pro Lys Asp Gly
 385 390 395 400

Arg Leu Leu Tyr Arg Pro Asn Lys Ala Gly Glu Thr Pro Tyr Asn Ile
 405 410 415

Asp Cys Ser His Gln Lys Ser Ile Leu Thr Gln Ile Phe Gly Ala Arg
 420 425 430

Protein Complexes associated with APP-processing

His Leu Ser Pro Thr Glu Thr Asp Gly Asp Met Leu Gly Tyr Asp Leu
 435 440 445

Tyr Ser Ser Ala Leu Ala Asp Ile Leu Ser Glu Pro Thr Met Gln Pro
 450 455 460

Pro Ile Cys Val Gly Leu Tyr Ala Gln Trp Gly Ser Gly Lys Ser Phe
 465 470 475 480

Leu Leu Lys Lys Leu Glu Asp Glu Met Lys Thr Phe Ala Gly Gln Gln
 485 490 495

Ile Glu Pro Leu Phe Gln Phe Ser Trp Leu Ile Val Phe Leu Thr Leu
 500 505 510

Leu Leu Cys Gly Gly Leu Gly Leu Leu Phe Ala Phe Thr Val His Pro
 515 520 525

Asn Leu Gly Ile Ala Val Ser Leu Ser Phe Leu Ala Leu Leu Tyr Ile
 530 535 540

Phe Phe Ile Val Ile Tyr Phe Gly Gly Arg Arg Glu Gly Glu Ser Trp
 545 550 555 560

Asn Trp Ala Trp Val Leu Ser Thr Arg Leu Ala Arg His Ile Gly Tyr
 565 570 575

Leu Glu Leu Leu Leu Lys Leu Met Phe Val Asn Pro Pro Glu Leu Pro
 580 585 590

Glu Gln Thr Thr Lys Ala Leu Pro Val Arg Phe Leu Phe Thr Asp Tyr
 595 600 605

Asn Arg Leu Ser Ser Val Gly Gly Glu Thr Ser Leu Ala Glu Met Ile
 610 615 620

Ala Thr Leu Ser Asp Ala Cys Glu Arg Glu Phe Gly Phe Leu Ala Thr
 625 630 635 640

Arg Leu Phe Arg Val Phe Lys Thr Glu Asp Thr Gln Gly Lys Lys Lys
 645 650 655

Trp Lys Lys Thr Cys Cys Leu Pro Ser Phe Val Ile Phe Leu Phe Ile
 660 665 670

Ile Gly Cys Ile Ile Ser Gly Ile Thr Leu Leu Ala Ile Phe Arg Val
 675 680 685

Asp Pro Lys His Leu Thr Val Asn Ala Val Leu Ile Ser Ile Ala Ser
 690 695 700

Protein Complexes associated with APP-processing

Val Val Gly Leu Ala Phe Val Leu Asn Cys Arg Thr Trp Trp Gln Val
705 710 715 720

Leu Asp Ser Leu Leu Asn Ser Gln Arg Lys Arg Leu His Asn Ala Ala
725 730 735

Ser Lys Leu His Lys Leu Lys Ser Glu Gly Phe Met Lys Val Leu Lys
740 745 750

Cys Glu Val Glu Leu Met Ala Arg Met Ala Lys Thr Ile Asp Ser Phe
755 760 765

Thr Gln Asn Gln Thr Arg Leu Val Val Ile Ile Asp Gly Leu Asp Ala
770 775 780

Cys Glu Gln Asp Lys Val Leu Gln Met Leu Asp Thr Val Arg Val Leu
785 790 795 800

Phe Ser Lys Gly Pro Phe Ile Ala Ile Phe Ala Ser Asp Pro His Ile
805 810 815

Ile Ile Lys Ala Ile Asn Gln Asn Leu Asn Ser Val Leu Arg Asp Ser
820 825 830

Asn Ile Asn Gly His Asp Tyr Met Arg Asn Ile Val His Leu Pro Val
835 840 845

Phe Leu Asn Ser Arg Gly Leu Ser Asn Ala Arg Lys Phe Leu Val Thr
850 855 860

Ser Ala Thr Asn Gly Asp Val Pro Cys Ser Asp Thr Thr Gly Ile Gln
865 870 875 880

Glu Asp Ala Asp Arg Arg Val Ser Gln Asn Ser Leu Gly Glu Met Thr
885 890 895

Lys Leu Gly Ser Lys Thr Ala Leu Asn Arg Arg Asp Thr Tyr Arg Arg
900 905 910

Arg Gln Met Gln Arg Thr Ile Thr Arg Gln Met Ser Phe Asp Leu Thr
915 920 925

Lys Leu Leu Val Thr Glu Asp Trp Phe Ser Asp Ile Ser Pro Gln Thr
930 935 940

Met Arg Arg Leu Leu Asn Ile Val Ser Val Thr Gly Arg Leu Leu Arg
945 950 955 960

Ala Asn Gln Ile Ser Phe Asn Trp Asp Arg Leu Ala Ser Trp Ile Asn
965 970 975

Protein Complexes associated with APP-processing
 Leu Thr Glu Gln Trp Pro Tyr Arg Thr Ser Trp Leu Ile Leu Tyr Leu
 980 985 990

Glu Glu Thr Glu Gly Ile Pro Asp Gln Met Thr Leu Lys Thr Ile Tyr
 995 1000 1005

Glu Arg Ile Ser Lys Asn Ile Pro Thr Thr Lys Asp Val Glu Pro
 1010 1015 1020

Leu Leu Glu Ile Asp Gly Asp Ile Arg Asn Phe Glu Val Phe Leu
 1025 1030 1035

Ser Ser Arg Thr Pro Val Leu Val Ala Arg Asp Val Lys Val Phe
 1040 1045 1050

Leu Pro Cys Thr Val Asn Leu Asp Pro Lys Leu Arg Glu Ile Ile
 1055 1060 1065

Ala Asp Val Arg Ala Ala Arg Glu Gln Ile Ser Ile Gly Gly Leu
 1070 1075 1080

Ala Tyr Pro Pro Leu Pro Leu His Glu Gly Pro Pro Arg Ala Pro
 1085 1090 1095

Ser Gly Tyr Ser Gln Pro Pro Ser Val Cys Ser Ser Thr Ser Phe
 1100 1105 1110

Asn Gly Pro Phe Ala Gly Gly Val Val Ser Pro Gln Pro His Ser
 1115 1120 1125

Ser Tyr Tyr Ser Gly Met Thr Gly Pro Gln His Pro Phe Tyr Asn
 1130 1135 1140

Arg Pro Phe Phe Ala Pro Tyr Leu Tyr Thr Pro Arg Tyr Tyr Pro
 1145 1150 1155

Gly Gly Ser Gln His Leu Ile Ser Arg Pro Ser Val Lys Thr Ser
 1160 1165 1170

Leu Pro Arg Asp Gln Asn Asn Gly Leu Glu Val Ile Lys Glu Asp
 1175 1180 1185

Ala Ala Glu Gly Leu Ser Ser Pro Thr Asp Ser Ser Arg Gly Ser
 1190 1195 1200

Gly Pro Ala Pro Gly Pro Val Val Leu Leu Asn Ser Leu Asn Val
 1205 1210 1215

Asp Ala Val Cys Glu Lys Leu Lys Gln Ile Glu Gly Leu Asp Gln
 1220 1225 1230

Protein Complexes associated with APP-processing

Ser	Met	Leu	Pro	Gln	Tyr	Cys	Thr	Thr	Ile	Lys	Lys	Ala	Asn	Ile
	1235					1240					1245			
Asn	Gly	Arg	Val	Leu	Ala	Gln	Cys	Asn	Ile	Asp	Glu	Leu	Lys	Lys
	1250					1255					1260			
Glu	Met	Asn	Met	Asn	Phe	Gly	Asp	Trp	His	Leu	Phe	Arg	Ser	Thr
	1265					1270					1275			
Val	Leu	Glu	Met	Arg	Asn	Ala	Glu	Ser	His	Val	Val	Pro	Glu	Asp
	1280					1285					1290			
Pro	Arg	Phe	Leu	Ser	Glu	Ser	Ser	Ser	Gly	Pro	Ala	Pro	His	Gly
	1295					1300					1305			
Glu	Pro	Ala	Arg	Arg	Ala	Ser	His	Asn	Glu	Leu	Pro	His	Thr	Glu
	1310					1315					1320			
Leu	Ser	Ser	Gln	Thr	Pro	Tyr	Thr	Leu	Asn	Phe	Ser	Phe	Glu	Glu
	1325					1330					1335			
Leu	Asn	Thr	Leu	Gly	Leu	Asp	Glu	Gly	Ala	Pro	Arg	His	Ser	Asn
	1340					1345					1350			
Leu	Ser	Trp	Gln	Ser	Gln	Thr	Arg	Arg	Thr	Pro	Ser	Leu	Ser	Ser
	1355					1360					1365			
Leu	Asn	Ser	Gln	Asp	Ser	Ser	Ile	Glu	Ile	Ser	Lys	Leu	Thr	Asp
	1370					1375					1380			
Lys	Val	Gln	Ala	Glu	Tyr	Arg	Asp	Ala	Tyr	Arg	Glu	Tyr	Ile	Ala
	1385					1390					1395			
Gln	Met	Ser	Gln	Leu	Glu	Gly	Gly	Pro	Gly	Ser	Thr	Thr	Ile	Ser
	1400					1405					1410			
Gly	Arg	Ser	Ser	Pro	His	Ser	Thr	Tyr	Tyr	Met	Gly	Gln	Ser	Ser
	1415					1420					1425			
Ser	Gly	Gly	Ser	Ile	His	Ser	Asn	Leu	Glu	Gln	Glu	Lys	Gly	Lys
	1430					1435					1440			
Asp	Ser	Glu	Pro	Lys	Pro	Asp	Asp	Gly	Arg	Lys	Ser	Phe	Leu	Met
	1445					1450					1455			
Lys	Arg	Gly	Asp	Val	Ile	Asp	Tyr	Ser	Ser	Ser	Gly	Val	Ser	Thr
	1460					1465					1470			
Asn	Asp	Ala	Ser	Pro	Leu	Asp	Pro	Ile	Thr	Glu	Glu	Asp	Glu	Lys
	1475					1480					1485			

Protein Complexes associated with APP-processing

Ser Asp Gln Ser Gly Ser Lys Leu Leu Pro Gly Lys Lys Ser Ser
 1490 1495 1500

Glu Arg Ser Ser Leu Phe Gln Thr Asp Leu Lys Leu Lys Gly Ser
 1505 1510 1515

Gly Leu Arg Tyr Gln Lys Leu Pro Ser Asp Glu Asp Glu Ser Gly
 1520 1525 1530

Thr Glu Glu Ser Asp Asn Thr Pro Leu Leu Lys Asp Asp Lys Asp
 1535 1540 1545

Arg Lys Ala Glu Gly Lys Val Glu Arg Val Pro Lys Ser Pro Glu
 1550 1555 1560

His Ser Ala Glu Pro Ile Arg Thr Phe Ile Lys Ala Lys Glu Tyr
 1565 1570 1575

Leu Ser Asp Ala Leu Leu Asp Lys Lys Asp Ser Ser Asp Ser Gly
 1580 1585 1590

Val Arg Ser Ser Glu Ser Ser Pro Asn His Ser Leu His Asn Glu
 1595 1600 1605

Val Ala Asp Asp Ser Gln Leu Glu Lys Ala Asn Leu Ile Glu Leu
 1610 1615 1620

Glu Asp Asp Ser His Ser Gly Lys Arg Gly Ile Pro His Ser Leu
 1625 1630 1635

Ser Gly Leu Gln Asp Pro Ile Ile Ala Arg Met Ser Ile Cys Ser
 1640 1645 1650

Glu Asp Lys Lys Ser Pro Ser Glu Cys Ser Leu Ile Ala Ser Ser
 1655 1660 1665

Pro Glu Glu Asn Trp Pro Ala Cys Gln Lys Ala Tyr Asn Leu Asn
 1670 1675 1680

Arg Thr Pro Ser Thr Val Thr Leu Asn Asn Asn Ser Ala Pro Ala
 1685 1690 1695

Asn Arg Ala Asn Gln Asn Phe Asp Glu Met Glu Gly Ile Arg Glu
 1700 1705 1710

Thr Ser Gln Val Ile Leu Arg Pro Ser Ser Ser Pro Asn Pro Thr
 1715 1720 1725

Thr Ile Gln Asn Glu Asn Leu Lys Ser Met Thr His Lys Arg Ser
 1730 1735 1740

Protein Complexes associated with APP-processing

Gln Arg Ser Ser Tyr Thr Arg Leu Ser Lys Asp Pro Pro Glu Leu
 1745 1750 1755

His Ala Ala Ala Ser Ser Glu Ser Thr Gly Phe Gly Glu Glu Arg
 1760 1765 1770

Glu Ser Ile Leu
 1775

<210> 195

<211> 546

<212> PRT

<213> Homo sapiens

<400> 195

Met Gly Ala Tyr Leu Ser Gln Pro Asn Thr Val Lys Cys Ser Gly Asp
 1 5 10 15

Gly Val Gly Ala Pro Arg Leu Pro Leu Pro Tyr Gly Phe Ser Ala Met
 20 25 30

Gln Gly Trp Arg Val Ser Met Glu Asp Ala His Asn Cys Ile Pro Glu
 35 40 45

Leu Asp Ser Glu Thr Ala Met Phe Ser Val Tyr Asp Gly His Gly Gly
 50 55 60

Glu Glu Val Ala Leu Tyr Cys Ala Lys Tyr Leu Pro Asp Ile Ile Lys
 65 70 75 80

Asp Gln Lys Ala Tyr Lys Glu Gly Lys Leu Gln Lys Ala Leu Glu Asp
 85 90 95

Ala Phe Leu Ala Ile Asp Ala Lys Leu Thr Thr Glu Glu Val Ile Lys
 100 105 110

Glu Leu Ala Gln Ile Ala Gly Arg Pro Thr Glu Asp Glu Asp Glu Lys
 115 120 125

Glu Lys Val Ala Asp Glu Asp Asp Val Asp Asn Glu Glu Ala Ala Leu
 130 135 140

Leu His Glu Glu Ala Thr Met Thr Ile Glu Glu Leu Leu Thr Arg Tyr
 145 150 155 160

Gly Gln Asn Cys His Lys Gly Pro Pro His Ser Lys Ser Gly Gly Gly
 165 170 175

Protein Complexes associated with APP-processing
 Thr Gly Glu Glu Pro Gly Ser Gln Gly Leu Asn Gly Glu Ala Gly Pro
 180 185 190

Lys Ala Tyr Thr Gly Phe Ser Ser Asn Ser Glu Arg Gly Thr Glu Ala
210 215 220

Cys Ser Ser Ala Ser Asp Lys Leu Pro Arg Val Ala Lys Ser Lys Phe
245 250 255

Asp Ser Glu Glu Cys Ser Glu Glu Glu Asp Gly Tyr Ser Ser Glu Glu
275 280 285

Asp Glu Glu Glu Glu Glu Glu Met Met Val Pro Gly Met Glu Gly Lys
305 310 315 320

Arg Gly Lys Gln Leu Ile Val Ala Asn Ala Gly Asp Ser Arg Cys Val
340 345 350

Glu Asp Glu Val Glu Leu Ala Arg Ile Lys Asn Ala Gly Gly Lys Val
370 375 380

Gly Asp His Phe Tyr Lys Arg Asn Lys Asn Leu Pro Pro Glu Glu Gln
405 410 415

His Glu Phe Met Val Ile Ala Cys Asp Gly Ile Trp Asn Val Met Ser
435 440 445

Protein Complexes associated with APP-processing
 Ser Gln Glu Val Val Asp Phe Ile Gln Ser Lys Ile Ser Gln Arg Asp
 450 455 460

Glu Asn Gly Glu Leu Arg Leu Leu Ser Ser Ile Val Glu Glu Leu Leu
 465 470 475 480

Asp Gln Cys Leu Ala Pro Asp Thr Ser Gly Asp Gly Thr Gly Cys Asp
 485 490 495

Asn Met Thr Cys Ile Ile Ile Cys Phe Lys Pro Arg Asn Thr Ala Glu
 500 505 510

Leu Gln Pro Glu Ser Gly Lys Arg Lys Leu Glu Glu Val Leu Ser Thr
 515 520 525

Glu Gly Ala Glu Glu Asn Gly Asn Ser Asp Lys Lys Lys Lys Ala Lys
 530 535 540

Arg Asp
 545

<210> 196

<211> 1069

<212> PRT

<213> Homo sapiens

<400> 196

Met Leu Arg Met Arg Thr Ala Gly Trp Ala Arg Gly Trp Cys Leu Gly
 1 5 10 15

Cys Cys Leu Leu Leu Pro Leu Ser Phe Ser Leu Ala Ala Ala Lys Gln
 20 25 30

Leu Leu Arg Tyr Arg Leu Ala Glu Glu Gly Pro Ala Asp Val Arg Ile
 35 40 45

Gly Asn Val Ala Ser Asp Leu Gly Ile Val Thr Gly Ser Gly Glu Val
 50 55 60

Thr Phe Ser Leu Glu Ser Gly Ser Glu Tyr Leu Lys Ile Asp Asn Leu
 65 70 75 80

Thr Gly Glu Leu Ser Thr Ser Glu Arg Arg Ile Asp Arg Glu Lys Leu
 85 90 95

Pro Gln Cys Gln Met Ile Phe Asp Glu Asn Glu Cys Phe Leu Asp Phe
 100 105 110

Protein Complexes associated with APP-processing

Glu Val Ser Val Ile Gly Pro Ser Gln Ser Trp Val Asp Leu Phe Glu
115 120 125

Gly Gln Val Ile Val Leu Asp Ile Asn Asp Asn Thr Pro Thr Phe Pro
130 135 140

Ser Pro Val Leu Thr Leu Thr Val Glu Glu Asn Arg Pro Val Gly Thr
145 150 155 160

Leu Tyr Leu Leu Pro Thr Ala Thr Asp Arg Asp Phe Gly Arg Asn Gly
165 170 175

Ile Glu Arg Tyr Glu Leu Leu Gln Glu Pro Gly Gly Gly Gly Ser Gly
180 185 190

Gly Glu Ser Arg Arg Ala Gly Ala Ala Asp Ser Ala Pro Tyr Pro Gly
195 200 205

Gly Gly Gly Asn Gly Ala Ser Gly Gly Gly Ser Gly Gly Ser Lys Arg
210 215 220

Arg Leu Asp Ala Ser Glu Gly Gly Gly Gly Thr Asn Pro Gly Gly Arg
225 230 235 240

Ser Ser Val Phe Glu Leu Gln Val Ala Asp Thr Pro Asp Gly Glu Lys
245 250 255

Gln Pro Gln Leu Ile Val Lys Gly Ala Leu Asp Arg Glu Gln Arg Asp
260 265 270

Ser Tyr Glu Leu Thr Leu Arg Val Arg Asp Gly Gly Asp Pro Pro Arg
275 280 285

Ser Ser Gln Ala Ile Leu Arg Val Leu Ile Thr Asp Val Asn Asp Asn
290 295 300

Ser Pro Arg Phe Glu Lys Ser Val Tyr Glu Ala Asp Leu Ala Glu Asn
305 310 315 320

Ser Ala Pro Gly Thr Pro Ile Leu Gln Leu Arg Ala Ala Asp Leu Asp
325 330 335

Val Gly Val Asn Gly Gln Ile Glu Tyr Val Phe Gly Ala Ala Thr Glu
340 345 350

Ser Val Arg Arg Leu Leu Arg Leu Asp Glu Thr Ser Gly Trp Leu Ser
355 360 365

Val Leu His Arg Ile Asp Arg Glu Glu Val Asn Gln Leu Arg Phe Thr
370 375 380

Protein Complexes associated with APP-processing

Val Met Ala Arg Asp Arg Gly Gln Pro Pro Lys Thr Asp Lys Ala Thr
 385 390 395 400

Val Val Leu Asn Ile Lys Asp Glu Asn Asp Asn Val Pro Ser Ile Glu
 405 410 415

Ile Arg Lys Ile Gly Arg Ile Pro Leu Lys Asp Gly Val Ala Asn Val
 420 425 430

Ala Glu Asp Val Leu Val Asp Thr Pro Ile Ala Leu Val Gln Val Ser
 435 440 445

Asp Arg Asp Gln Gly Glu Asn Gly Val Val Thr Cys Thr Val Val Gly
 450 455 460

Asp Val Pro Phe Gln Leu Lys Pro Ala Ser Asp Thr Glu Gly Asp Gln
 465 470 475 480

Asn Lys Lys Lys Tyr Phe Leu His Thr Ser Thr Pro Leu Asp Tyr Glu
 485 490 495

Ala Thr Arg Glu Phe Asn Val Val Ile Val Ala Val Asp Ser Gly Ser
 500 505 510

Pro Ser Leu Ser Ser Lys Asn Ser Leu Ile Val Lys Val Gly Asp Thr
 515 520 525

Asn Asp Asn Pro Pro Met Phe Gly Gln Ser Val Val Glu Val Tyr Phe
 530 535 540

Pro Glu Asn Asn Ile Pro Gly Glu Arg Val Ala Thr Val Leu Ala Thr
 545 550 555 560

Asp Ala Asp Ser Gly Lys Asn Ala Glu Ile Ala Tyr Ser Leu Asp Ser
 565 570 575

Ser Val Met Gly Ile Phe Ala Ile Asp Pro Asp Ser Gly Asp Ile Leu
 580 585 590

Val Asn Thr Val Leu Asp Arg Glu Gln Thr Asp Arg Tyr Glu Phe Lys
 595 600 605

Val Asn Ala Lys Asp Lys Gly Ile Pro Val Leu Gln Gly Ser Thr Thr
 610 615 620

Val Ile Val Gln Val Ala Asp Lys Asn Asp Asn Asp Pro Lys Phe Met
 625 630 635 640

Gln Asp Val Phe Thr Phe Tyr Val Lys Glu Asn Leu Gln Pro Asn Ser
 645 650 655

Protein Complexes associated with APP-processing

Pro Val Gly Met Val Thr Val Met Asp Ala Asp Lys Gly Arg Asn Ala
660 665 670

Glu Met Ser Leu Tyr Ile Glu Glu Asn Asn Asn Ile Phe Ser Ile Glu
675 680 685

Asn Asp Thr Gly Thr Ile Tyr Ser Thr Met Ser Phe Asp Arg Glu His
690 695 700

Gln Thr Thr Tyr Thr Phe Arg Val Lys Ala Val Asp Gly Gly Asp Pro
705 710 715 720

Pro Arg Ser Ala Thr Ala Thr Val Ser Leu Phe Val Met Asp Glu Asn
725 730 735

Asp Asn Ala Pro Thr Val Thr Leu Pro Lys Asn Ile Ser Tyr Thr Leu
740 745 750

Leu Pro Pro Ser Ser Asn Val Arg Thr Val Val Ala Thr Val Leu Ala
755 760 765

Thr Asp Ser Asp Asp Gly Ile Asn Ala Asp Leu Asn Tyr Ser Ile Val
770 775 780

Gly Gly Asn Pro Phe Lys Leu Phe Glu Ile Asp Pro Thr Ser Gly Val
785 790 795 800

Val Ser Leu Val Gly Lys Leu Thr Gln Lys His Tyr Gly Leu His Arg
805 810 815

Leu Val Val Gln Val Asn Asp Ser Gly Gln Pro Ser Gln Ser Thr Thr
820 825 830

Thr Val Val His Val Phe Val Asn Glu Ser Val Ser Asn Ala Thr Ala
835 840 845

Ile Asp Ser Gln Ile Ala Arg Ser Leu His Ile Pro Leu Thr Gln Asp
850 855 860

Ile Ala Gly Asp Pro Ser Tyr Glu Ile Ser Lys Gln Arg Leu Ser Ile
865 870 875 880

Val Ile Gly Val Val Ala Gly Ile Met Thr Val Ile Leu Ile Ile Leu
885 890 895

Ile Val Val Met Ala Arg Tyr Cys Arg Ser Lys Asn Lys Asn Gly Tyr
900 905 910

Glu Ala Gly Lys Lys Asp His Glu Asp Phe Phe Thr Pro Gln Gln His
915 920 925

Protein Complexes associated with APP-processing

Asp Lys Ser Lys Lys Pro Lys Lys Asp Lys Lys Asn Lys Lys Ser Lys
 930 935 940

Gln Pro Leu Tyr Ser Ser Ile Val Thr Val Glu Ala Ser Lys Pro Asn
 945 950 955 960

Gly Gln Arg Tyr Asp Ser Val Asn Glu Lys Leu Ser Asp Ser Pro Ser
 965 970 975

Met Gly Arg Tyr Arg Ser Val Asn Gly Gly Pro Gly Ser Pro Asp Leu
 980 985 990

Ala Arg His Tyr Lys Ser Ser Ser Pro Leu Pro Thr Val Gln Leu His
 995 1000 1005

Pro Gln Ser Pro Thr Ala Gly Lys Lys His Gln Ala Val Gln Asp
 1010 1015 1020

Leu Pro Pro Ala Asn Thr Phe Val Gly Ala Gly Asp Asn Ile Ser
 1025 1030 1035

Ile Gly Ser Asp His Cys Ser Glu Tyr Ser Cys Gln Thr Asn Asn
 1040 1045 1050

Lys Tyr Ser Lys Gln Met Arg Leu His Pro Tyr Ile Thr Val Phe
 1055 1060 1065

Gly

<210> 197

<211> 776

<212> PRT

<213> Homo sapiens

<400> 197

Met Glu Ile Gly Trp Met His Asn Arg Arg Gln Arg Gln Val Leu Val
 1 5 10 15

Phe Phe Val Leu Leu Ser Leu Ser Gly Ala Gly Ala Glu Leu Gly Ser
 20 25 30

Tyr ser val val Glu Glu Thr Glu Arg Gly Ser Phe val Ala Asn Leu
 35 40 45

Gly Lys Asp Leu Gly Leu Gly Leu Thr Glu Met Ser Thr Arg Lys Ala
 50 55 60

Protein Complexes associated with APP-processing

Arg Ile Ile Ser Gln Gly Asn Lys Gln His Leu Gln Leu Lys Ala Gln
 65 70 75 80

Thr Gly Asp Leu Leu Ile Asn Glu Lys Leu Asp Arg Glu Glu Leu Cys
 85 90 95

Gly Pro Thr Glu Pro Cys Ile Leu His Phe Gln Val Leu Met Glu Asn
 100 105 110

Pro Leu Glu Ile Phe Gln Ala Glu Leu Arg Val Ile Asp Ile Asn Asp
 115 120 125

His Ser Pro Met Phe Thr Glu Lys Glu Met Ile Leu Lys Ile Pro Glu
 130 135 140

Asn Ser Pro Leu Gly Thr Glu Phe Pro Leu Asn His Ala Leu Asp Leu
 145 150 155 160

Asp Val Gly Ser Asn Asn Val Gln Asn Tyr Lys Ile Ser Pro Ser Ser
 165 170 175

His Phe Arg Val Leu Ile His Glu Phe Arg Asp Gly Arg Lys Tyr Pro
 180 185 190

Glu Leu Val Leu Asp Lys Glu Leu Asp Arg Glu Glu Glu Pro Gln Leu
 195 200 205

Arg Leu Thr Leu Thr Ala Leu Asp Gly Gly Ser Pro Pro Arg Ser Gly
 210 215 220

Thr Ala Gln Val Arg Ile Glu Val Val Asp Ile Asn Asp Asn Ala Pro
 225 230 235 240

Glu Phe Glu Gln Pro Ile Tyr Lys Val Gln Ile Pro Glu Asn Ser Pro
 245 250 255

Leu Gly Ser Leu Val Ala Thr Val Ser Ala Arg Asp Leu Asp Gly Gly
 260 265 270

Ala Asn Gly Lys Ile Ser Tyr Thr Leu Phe Gln Pro Ser Glu Asp Ile
 275 280 285

Ser Lys Thr Leu Glu Val Asn Pro Met Thr Gly Glu Val Arg Leu Arg
 290 295 300

Lys Gln Val Asp Phe Glu Met Val Thr Ser Tyr Glu Val Arg Ile Lys
 305 310 315 320

Ala Thr Asp Gly Gly Gly Leu Ser Gly Lys Cys Thr Leu Leu Leu Gln
 325 330 335

Protein Complexes associated with APP-processing

Val Val Asp Val Asn Asp Asn Pro Pro Gln Val Thr Met Ser Ala Leu
340 345 350

Thr Ser Pro Ile Pro Glu Asn Ser Pro Glu Ile Val Val Ala Val Phe
355 360 365

Ser Val Ser Asp Pro Asp Ser Gly Asn Asn Gly Lys Thr Ile Ser Ser
370 375 380

Ile Gln Glu Asp Leu Pro Phe Leu Leu Lys Pro Ser Val Lys Asn Phe
385 390 395 400

Tyr Thr Leu Val Thr Glu Arg Ala Leu Asp Arg Glu Ala Arg Ala Glu
405 410 415

Tyr Asn Ile Thr Leu Thr Val Thr Asp Met Gly Thr Pro Arg Leu Lys
420 425 430

Thr Glu His Asn Ile Thr Val Gln Ile Ser Asp Val Asn Asp Asn Ala
435 440 445

Pro Thr Phe Thr Gln Thr Ser Tyr Thr Leu Phe Val Arg Glu Asn Asn
450 455 460

Ser Pro Ala Leu His Ile Gly Ser Val Ser Ala Thr Asp Arg Asp Ser
465 470 475 480

Gly Thr Asn Ala Gln Val Thr Tyr Ser Leu Leu Pro Pro Gln Asp Pro
485 490 495

His Leu Pro Leu Ala Ser Leu Val Ser Ile Asn Ala Asp Asn Gly His
500 505 510

Leu Phe Ala Leu Arg Ser Leu Asp Tyr Glu Ala Leu Gln Ala Phe Glu
515 520 525

Phe Arg Val Gly Ala Thr Asp Arg Gly Ser Pro Ala Leu Ser Arg Glu
530 535 540

Ala Leu Val Arg Val Leu Val Leu Asp Ala Asn Asp Asn Ser Pro Phe
545 550 555 560

Val Leu Tyr Pro Leu Gln Asn Gly Ser Ala Pro Cys Thr Glu Leu Val
565 570 575

Pro Arg Ala Ala Glu Pro Gly Tyr Leu Val Thr Lys Val Val Ala Val
580 585 590

Asp Gly Asp Ser Gly Gln Asn Ala Trp Leu Ser Tyr Gln Leu Leu Lys
595 600 605

Protein Complexes associated with APP-processing
 Ala Thr Glu Pro Gly Leu Phe Gly Val Trp Ala His Asn Gly Glu Val
 610 615 620

Arg Thr Ala Arg Leu Leu Ser Glu Arg Asp Ala Ala Lys Gln Arg Leu
 625 630 635 640

Val Val Leu Val Lys Asp Asn Gly Glu Pro Pro Arg Ser Ala Thr Ala
 645 650 655

Thr Leu His Val Leu Leu Val Asp Gly Phe Ser Gln Pro Phe Leu Pro
 660 665 670

Leu Pro Glu Ala Ala Pro Gly Gln Thr Gln Ala Asn Ser Leu Thr Val
 675 680 685

Tyr Leu Val Val Ala Leu Ala Ser Val Ser Ser Leu Phe Leu Phe Ser
 690 695 700

Val Leu Leu Phe Val Ala Val Arg Leu Cys Arg Arg Ser Arg Ala Ala
 705 710 715 720

Ser Val Gly Arg Cys Ser Met Pro Glu Gly Pro Phe Pro Gly Arg Leu
 725 730 735

Val Asp Val Ser Gly Thr Gly Thr Leu Ser Gln Ser Tyr Gln Tyr Glu
 740 745 750

Val Cys Leu Thr Gly Gly Ser Glu Thr Ser Glu Phe Lys Phe Leu Lys
 755 760 765

Pro Ile Ile Pro Asn Phe Ser Pro
 770 775

<210> 198

<211> 206

<212> PRT

<213> Homo sapiens

<400> 198

Met Asp Glu Asp Val Leu Thr Thr Leu Lys Ile Leu Ile Ile Gly Glu
 1 5 10 15

Ser Gly Val Gly Lys Ser Ser Leu Leu Arg Phe Thr Asp Asp Thr
 20 25 30

Phe Asp Pro Glu Leu Ala Ala Thr Ile Gly Val Asp Phe Lys Val Lys
 35 40 45

Protein Complexes associated with APP-processing
 Thr Ile Ser Val Asp Gly Asn Lys Ala Lys Leu Ala Ile Trp Asp Thr
 50 55 60

Ala Gly Gln Glu Arg Phe Arg Thr Leu Thr Pro Ser Tyr Tyr Arg Gly
 65 70 75 80

Ala Gln Gly Val Ile Leu Val Tyr Asp Val Thr Arg Arg Asp Thr Phe
 85 90 95

Val Lys Leu Asp Asn Trp Leu Asn Glu Leu Glu Thr Tyr Cys Thr Arg
 100 105 110

Asn Asp Ile Val Asn Met Leu Val Gly Asn Lys Ile Asp Lys Glu Asn
 115 120 125

Arg Glu Val Asp Arg Asn Glu Gly Leu Lys Phe Ala Arg Lys His Ser
 130 135 140

Met Leu Phe Ile Glu Ala Ser Ala Lys Thr Cys Asp Gly Val Gln Cys
 145 150 155 160

Ala Phe Glu Glu Leu Val Glu Lys Ile Ile Gln Thr Pro Gly Leu Trp
 165 170 175

Glu Ser Glu Asn Gln Asn Lys Gly Val Lys Leu Ser His Arg Glu Glu
 180 185 190

Gly Gln Gly Gly Gly Ala Cys Gly Gly Tyr Cys Ser Val Leu
 195 200 205

<210> 199

<211> 1393

<212> PRT

<213> Homo sapiens

<400> 199

Met Ala Cys Ser Ile Val Gln Phe Cys Tyr Phe Gln Asp Leu Gln Ala
 1 5 10 15

Ala Arg Asp Phe Leu Phe Pro His Leu Arg Glu Glu Ile Leu Ser Gly
 20 25 30

Ala Leu Arg Arg Asp Pro Ser Lys Ser Thr Asp Trp Glu Asp Asp Gly
 35 40 45

Trp Gly Ala Trp Glu Glu Asn Glu Pro Gln Glu Pro Glu Glu Glu Gly
 50 55 60

Protein Complexes associated with APP-processing

Asn Thr Cys Lys Thr Gln Lys Thr Ser Trp Leu Gln Asp Cys Val Leu
 65 70 75 80

Ser Leu Ser Pro Thr Asn Asp Leu Met Val Ile Ala Arg Glu Gln Lys
 85 90 95

Ala Val Phe Leu Val Pro Lys Trp Lys Tyr Ser Asp Lys Gly Lys Glu
 100 105 110

Glu Met Gln Phe Ala Val Gly Trp Ser Gly Ser Leu Asn Val Glu Glu
 115 120 125

Gly Glu Cys Val Thr Ser Ala Leu Cys Ile Pro Leu Ala Ser Gln Lys
 130 135 140

Arg Ser Ser Thr Gly Arg Pro Asp Trp Thr Cys Ile Val Val Gly Phe
 145 150 155 160

Thr Ser Gly Tyr Val Arg Phe Tyr Thr Glu Asn Gly Val Leu Leu Leu
 165 170 175

Ala Gln Leu Leu Asn Glu Asp Pro Val Leu Gln Leu Lys Cys Arg Thr
 180 185 190

Tyr Glu Ile Pro Arg His Pro Gly Val Thr Glu Gln Asn Glu Glu Leu
 195 200 205

Ser Ile Leu Tyr Pro Ala Ala Ile Val Thr Ile Asp Gly Phe Ser Leu
 210 215 220

Phe Gln Ser Leu Arg Ala Cys Arg Asn Gln Val Ala Lys Ala Ala Ala
 225 230 235 240

Ser Gly Asn Glu Asn Ile Gln Pro Pro Pro Leu Ala Tyr Lys Lys Trp
 245 250 255

Gly Leu Gln Asp Ile Asp Thr Ile Ile Asp His Ala Ser Val Gly Ile
 260 265 270

Met Thr Leu Ser Pro Phe Asp Gln Met Lys Thr Ala Ser Asn Ile Gly
 275 280 285

Gly Phe Asn Ala Ala Ile Lys Asn Ser Pro Pro Ala Met Ser Gln Tyr
 290 295 300

Ile Thr Val Gly Ser Asn Pro Phe Thr Gly Phe Phe Tyr Ala Leu Glu
 305 310 315 320

Gly Ser Thr Gln Pro Leu Leu Ser His Val Ala Leu Ala Val Ala Ser
 325 330 335

Protein Complexes associated with APP-processing
 Lys Leu Thr Ser Ala Leu Phe Asn Ala Ala Ser Gly Trp Leu Gly Trp
 340 345 350

Lys Ser Lys His Glu Glu Glu Ala Val Gln Lys Gln Lys Pro Lys Val
 355 360 365

Glu Pro Ala Thr Pro Leu Ala Val Arg Phe Gly Leu Pro Asp Ser Arg
 370 375 380

Arg His Gly Glu Ser Ile Cys Leu Ser Pro Cys Asn Thr Leu Ala Ala
 385 390 395 400

Val Thr Asp Asp Phe Gly Arg Val Ile Leu Leu Asp Val Ala Arg Gly
 405 410 415

Ile Ala Ile Arg Met Trp Lys Gly Tyr Arg Asp Ala Gln Ile Gly Trp
 420 425 430

Ile Gln Thr Val Glu Asp Leu His Glu Arg Val Pro Glu Lys Ala Asp
 435 440 445

Phe Ser Pro Phe Gly Asn Ser Gln Gly Pro Ser Arg Val Ala Gln Phe
 450 455 460

Leu Val Ile Tyr Ala Pro Arg Arg Gly Ile Leu Glu Val Trp Ser Thr
 465 470 475 480

Gln Gln Gly Pro Arg Val Gly Ala Phe Asn Val Gly Lys His Cys Arg
 485 490 495

Leu Leu Tyr Pro Gly Tyr Lys Ile Met Gly Leu Asn Asn Val Thr Ser
 500 505 510

Gln Ser Trp Gln Pro Gln Thr Tyr Gln Ile Cys Leu Val Asp Pro Val
 515 520 525

Ser Gly Ser Val Lys Thr Val Asn Val Pro Phe His Leu Ala Leu Ser
 530 535 540

Asp Lys Lys Ser Glu Arg Ala Lys Asp Met His Leu Val Lys Lys Leu
 545 550 555 560

Ala Ala Leu Leu Lys Thr Lys Ser Pro Asn Leu Asp Leu Val Glu Thr
 565 570 575

Glu Ile Lys Glu Leu Ile Leu Asp Ile Lys Tyr Pro Ala Thr Lys Lys
 580 585 590

Gln Ala Leu Glu Ser Ile Leu Ala Ser Glu Arg Leu Pro Phe Ser Cys
 595 600 605

Protein Complexes associated with APP-processing

Leu Arg Asn Ile Thr Gln Thr Leu Met Asp Thr Leu Lys Ser Gln Glu
610 615 620

Leu Glu Ser Val Asp Glu Gly Leu Leu Gln Phe Cys Ala Asn Lys Leu
625 630 635 640

Lys Leu Leu Gln Leu Tyr Glu Ser Val Ser Gln Leu Asn Ser Leu Asp
645 650 655

Phe His Leu Asp Thr Pro Phe Ser Asp Asn Asp Leu Ala Leu Leu Leu
660 665 670

Arg Leu Asp Glu Lys Glu Leu Leu Lys Leu Gln Ala Leu Leu Glu Lys
675 680 685

Tyr Lys Gln Glu Asn Thr Arg Thr Asn Val Arg Phe Ser Asp Asp Lys
690 695 700

Asp Gly Val Leu Pro Val Lys Thr Phe Leu Glu Tyr Leu Glu Tyr Glu
705 710 715 720

Lys Asp Val Leu Asn Ile Lys Lys Ile Ser Glu Glu Glu Tyr Val Ala
725 730 735

Leu Gly Ser Phe Phe Phe Trp Lys Cys Leu His Gly Glu Ser Ser Thr
740 745 750

Glu Asp Met Cys His Thr Leu Glu Ser Ala Gly Leu Ser Pro Gln Leu
755 760 765

Leu Leu Ser Leu Leu Leu Ser Val Trp Leu Ser Lys Glu Lys Asp Ile
770 775 780

Leu Asp Lys Pro Gln Ser Ile Cys Cys Leu His Thr Met Leu Ser Leu
785 790 795 800

Leu Ser Lys Met Lys Val Ala Ile Asp Glu Thr Trp Asp Ser Gln Ser
805 810 815

Val Ser Pro Trp Trp Gln Gln Met Arg Thr Ala Cys Ile Gln Ser Glu
820 825 830

Asn Asn Gly Ala Ala Leu Leu Ser Ala His Val Gly His Ser Val Ala
835 840 845

Ala Gln Ile Ser Asn Asn Met Thr Glu Lys Lys Phe Ser Gln Thr Val
850 855 860

Leu Gly Ala Asp Ser Glu Ala Leu Thr Asp Ser Trp Glu Ala Leu Ser
865 870 875 880

Leu Asp Thr Glu Tyr Trp Lys Leu Leu Lys Gln Leu Glu Asp Cys
885 890 895

Asp Ala Trp Leu Ser Val Glu Gly Pro Ile Ser Ile Val Glu Leu
1130 1135 1140

Protein Complexes associated with APP-processing

Ala Leu Glu Gln Lys His Ile His Tyr Pro Leu Val Glu His His
 1145 1150 1155

Ser Ile Leu Cys Ser Ile Leu Tyr Ala Val Met Arg Phe Ser Leu
 1160 1165 1170

Lys Thr Val Lys Pro Leu Ser Leu Phe Asp Ser Lys Gly Lys Asn
 1175 1180 1185

Ala Phe Phe Lys Asp Leu Thr Ser Ile Gln Leu Leu Pro Ser Gly
 1190 1195 1200

Glu Met Asp Pro Asn Phe Ile Ser Val Arg Gln Gln Phe Leu Leu
 1205 1210 1215

Lys Val Val Ser Ala Ala Val Gln Ala Gln His Ser Ala Thr Lys
 1220 1225 1230

Val Lys Asp Pro Thr Glu Glu Ala Thr Pro Thr Pro Phe Gly Lys
 1235 1240 1245

Asp Gln Asp Trp Pro Ala Leu Ala Val Asp Leu Ala His His Leu
 1250 1255 1260

Gln Val Ser Glu Asp Val Val Arg Arg His Tyr Val Gly Glu Leu
 1265 1270 1275

Tyr Asn Tyr Gly Val Asp His Leu Gly Glu Glu Ala Ile Leu Gln
 1280 1285 1290

Val His Asp Lys Glu Val Leu Ala Ser Gln Leu Leu Val Leu Thr
 1295 1300 1305

Gly Gln Arg Leu Ala His Ala Leu Leu His Thr Gln Thr Lys Glu
 1310 1315 1320

Gly Met Glu Leu Leu Ala Arg Leu Pro Pro Thr Leu Cys Thr Trp
 1325 1330 1335

Leu Lys Ala Met Asp Pro Gln Asp Leu Gln Asn Thr Glu Val Pro
 1340 1345 1350

Ile Ala Thr Thr Ala Lys Leu Val Asn Lys Val Ile Glu Leu Leu
 1355 1360 1365

Pro Glu Lys His Gly Gln Tyr Gly Leu Ala Leu His Leu Ile Glu
 1370 1375 1380

Ala Val Glu Ala Ile Ser Leu Pro Ser Leu
 1385 1390

Protein Complexes associated with APP-processing

<210> 200

<211> 944

<212> PRT

<213> Homo sapiens

<400> 200

Met Thr Val Ser Gly Pro Gly Thr Pro Glu Pro Arg Pro Ala Thr Pro
 1 5 10 15

Gly Ala Ser Ser Val Glu Gln Leu Arg Lys Glu Gly Asn Glu Leu Phe
 20 25 30

Lys Cys Gly Asp Tyr Gly Gly Ala Leu Ala Ala Tyr Thr Gln Ala Leu
 35 40 45

Gly Leu Asp Ala Thr Pro Gln Asp Gln Ala Val Leu His Arg Asn Arg
 50 55 60

Ala Ala Cys His Leu Lys Leu Glu Asp Tyr Asp Lys Ala Glu Thr Glu
 65 70 75 80

Ala Ser Lys Ala Ile Glu Lys Asp Gly Gly Asp Val Lys Ala Leu Tyr
 85 90 95

Arg Arg Ser Gln Ala Leu Glu Lys Leu Gly Arg Leu Asp Gln Ala Val
 100 105 110

Leu Asp Leu Gln Arg Cys Val Ser Leu Glu Pro Lys Asn Lys Val Phe
 115 120 125

Gln Glu Ala Leu Arg Asn Ile Gly Gly Gln Ile Gln Glu Lys Val Arg
 130 135 140

Tyr Met Ser Ser Thr Asp Ala Lys Val Glu Gln Met Phe Gln Ile Leu
 145 150 155 160

Leu Asp Pro Glu Glu Lys Gly Thr Glu Lys Lys Gln Lys Ala Ser Gln
 165 170 175

Asn Leu Val Val Leu Ala Arg Glu Asp Ala Gly Ala Glu Lys Ile Phe
 180 185 190

Arg Ser Asn Gly Val Gln Leu Leu Gln Arg Leu Leu Asp Met Gly Glu
 195 200 205

Thr Asp Leu Met Leu Ala Ala Leu Arg Thr Leu Val Gly Ile Cys Ser
 210 215 220

Protein Complexes associated with APP-processing

Glu His Gln Ser Arg Thr Val Ala Thr Leu Ser Ile Leu Gly Thr Arg
 225 230 235 240

Arg Val Val Ser Ile Leu Gly Val Glu Ser Gln Ala Val Ser Leu Ala
 245 250 255

Ala Cys His Leu Leu Gln Val Met Phe Asp Ala Leu Lys Glu Gly Val
 260 265 270

Lys Lys Gly Phe Arg Gly Lys Glu Gly Ala Ile Ile Val Asp Pro Ala
 275 280 285

Arg Glu Leu Lys Val Leu Ile Ser Asn Leu Leu Asp Leu Leu Thr Glu
 290 295 300

Val Gly Val Ser Gly Gln Gly Arg Asp Asn Ala Leu Thr Leu Leu Ile
 305 310 315 320

Lys Ala Val Pro Arg Lys Ser Leu Lys Asp Pro Asn Asn Ser Leu Thr
 325 330 335

Leu Trp Val Ile Asp Gln Gly Leu Lys Lys Ile Leu Glu Val Gly Gly
 340 345 350

Ser Leu Gln Asp Pro Pro Gly Glu Leu Ala Val Thr Ala Asn Ser Arg
 355 360 365

Met Ser Ala Ser Ile Leu Leu Ser Lys Leu Phe Asp Asp Leu Lys Cys
 370 375 380

Asp Ala Glu Arg Glu Asn Phe His Arg Leu Cys Glu Asn Tyr Ile Lys
 385 390 395 400

Ser Trp Phe Glu Gly Gln Gly Leu Ala Gly Lys Leu Arg Ala Ile Gln
 405 410 415

Thr Val Ser Cys Leu Leu Gln Gly Pro Cys Asp Ala Gly Asn Arg Ala
 420 425 430

Leu Glu Leu Ser Gly Val Met Glu Ser Val Ile Ala Leu Cys Ala Ser
 435 440 445

Glu Gln Glu Glu Glu Gln Leu Val Ala Val Glu Ala Leu Ile His Ala
 450 455 460

Ala Gly Lys Ala Lys Arg Ala Ser Phe Ile Thr Ala Asn Gly Val Ser
 465 470 475 480

Leu Leu Lys Asp Leu Tyr Lys Cys Ser Glu Lys Asp Ser Ile Arg Ile
 485 490 495

Protein Complexes associated with APP-processing

Arg Ala Leu Val Gly Leu Cys Lys Leu Gly Ser Ala Gly Gly Thr Asp
 500 505 510

Phe Ser Met Lys Gln Phe Ala Glu Gly Ser Thr Leu Lys Leu Ala Lys
 515 520 525

Gln Cys Arg Lys Trp Leu Cys Asn Asp Gln Ile Asp Ala Gly Thr Arg
 530 535 540

Arg Trp Ala Val Glu Gly Leu Ala Tyr Leu Thr Phe Asp Ala Asp Val
 545 550 555 560

Lys Glu Glu Phe Val Glu Asp Ala Ala Ala Leu Lys Ala Leu Phe Gln
 565 570 575

Leu Ser Arg Leu Glu Glu Arg Ser Val Leu Phe Ala Val Ala Ser Ala
 580 585 590

Leu Val Asn Cys Thr Asn Ser Tyr Asp Tyr Glu Glu Pro Asp Pro Lys
 595 600 605

Met Val Glu Leu Ala Lys Tyr Ala Lys Gln His Val Pro Glu Gln His
 610 615 620

Pro Lys Asp Lys Pro Ser Phe Val Arg Ala Arg Val Lys Lys Leu Leu
 625 630 635 640

Ala Ala Gly Val Val Ser Ala Met Val Cys Met Val Lys Thr Glu Ser
 645 650 655

Pro Val Leu Thr Ser Ser Cys Arg Glu Leu Leu Ser Arg Val Phe Leu
 660 665 670

Ala Leu Val Glu Glu Val Glu Asp Arg Gly Thr Val Val Ala Gln Gly
 675 680 685

Gly Gly Arg Ala Leu Ile Pro Leu Ala Leu Glu Gly Thr Asp Val Gly
 690 695 700

Gln Thr Lys Ala Ala Gln Ala Leu Ala Lys Leu Thr Ile Thr Ser Asn
 705 710 715 720

Pro Glu Met Thr Phe Pro Gly Glu Arg Ile Tyr Glu Val Val Arg Pro
 725 730 735

Leu Val Ser Leu Leu His Leu Asn Cys Ser Gly Leu Gln Asn Phe Glu
 740 745 750

Ala Leu Met Ala Leu Thr Asn Leu Ala Gly Ile Ser Glu Arg Leu Arg
 755 760 765

Protein Complexes associated with APP-processing
 Gln Lys Ile Leu Lys Glu Lys Ala Val Pro Met Ile Glu Gly Tyr Met
 770 775 780

Phe Glu Glu His Glu Met Ile Arg Arg Ala Ala Thr Glu Cys Met Cys
 785 790 795 800

Asn Leu Ala Met Ser Lys Glu Val Gln Asp Leu Phe Glu Ala Gln Gly
 805 810 815

Asn Asp Arg Leu Lys Leu Leu Val Leu Tyr Ser Gly Glu Asp Asp Glu
 820 825 830

Leu Leu Gln Arg Ala Ala Ala Gly Gly Leu Ala Met Leu Thr Ser Met
 835 840 845

Arg Pro Thr Leu Cys Ser Arg Ile Pro Gln Val Thr Thr His Trp Leu
 850 855 860

Glu Ile Leu Gln Ala Leu Leu Leu Ser Ser Asn Gln Glu Leu Gln His
 865 870 875 880

Arg Gly Ala Val Val Val Leu Asn Met Val Glu Ala Ser Arg Glu Ile
 885 890 895

Ala Ser Thr Leu Met Glu Ser Glu Met Met Glu Ile Leu Ser Val Leu
 900 905 910

Ala Lys Gly Asp His Ser Pro Val Thr Arg Ala Ala Ala Ala Cys Leu
 915 920 925

Asp Lys Ala Val Glu Tyr Gly Leu Ile Gln Pro Asn Gln Asp Gly Glu
 930 935 940

<210> 201

<211> 322

<212> PRT

<213> Homo sapiens

<400> 201

Met Ser Gly Glu Leu Pro Pro Asn Ile Asn Ile Lys Glu Pro Arg Trp
 1 5 10 15

Asp Gln Ser Thr Phe Ile Gly Arg Ala Asn His Phe Phe Thr Val Thr
 20 25 30

Asp Pro Arg Asn Ile Leu Leu Thr Asn Glu Gln Leu Glu Ser Ala Arg
 35 40 45

Protein Complexes associated with APP-processing
 Lys Ile Val His Asp Tyr Arg Gln Gly Ile Val Pro Pro Gly Leu Thr
 50 55 60

Glu Asn Glu Leu Trp Arg Ala Lys Tyr Ile Tyr Asp Ser Ala Phe His
 65 70 75 80

Pro Asp Thr Gly Glu Lys Met Ile Leu Ile Gly Arg Met Ser Ala Gln
 85 90 95

Val Pro Met Asn Met Thr Ile Thr Gly Cys Met Met Thr Phe Tyr Arg
 100 105 110

Thr Thr Pro Ala Val Leu Phe Trp Gln Trp Ile Asn Gln Ser Phe Asn
 115 120 125

Ala Val Val Asn Tyr Thr Asn Arg Ser Gly Asp Ala Pro Leu Thr Val
 130 135 140

Asn Glu Leu Gly Thr Ala Tyr Val Ser Ala Thr Thr Gly Ala Val Ala
 145 150 155 160

Thr Ala Leu Gly Leu Asn Ala Leu Thr Lys His Val Ser Pro Leu Ile
 165 170 175

Gly Arg Phe Val Pro Phe Ala Ala Val Ala Ala Ala Asn Cys Ile Asn
 180 185 190

Ile Pro Leu Met Arg Gln Arg Glu Leu Lys Val Gly Ile Pro Val Thr
 195 200 205

Asp Glu Asn Gly Asn Arg Leu Gly Glu Ser Ala Asn Ala Ala Lys Gln
 210 215 220

Ala Ile Thr Gln Val Val Val Ser Arg Ile Leu Met Ala Ala Pro Gly
 225 230 235 240

Met Ala Ile Pro Pro Phe Ile Met Asn Thr Leu Glu Lys Lys Ala Phe
 245 250 255

Leu Lys Arg Phe Pro Trp Met Ser Ala Pro Ile Gln Val Gly Leu Val
 260 265 270

Gly Phe Cys Leu Val Phe Ala Thr Pro Leu Cys Cys Ala Leu Phe Pro
 275 280 285

Gln Lys Ser Ser Met Ser Val Thr Ser Leu Glu Ala Glu Leu Gln Ala
 290 295 300

Lys Ile Gln Glu Ser His Pro Glu Leu Arg Arg Val Tyr Phe Asn Lys
 305 310 315 320

Protein Complexes associated with APP-processing

Gly Leu

<210> 202

<211> 750

<212> PRT

<213> Homo sapiens

<400> 202

Met Ser Gln Trp Tyr Glu Leu Gln Gln Leu Asp Ser Lys Phe Leu Glu
 1 5 10 15

Gln Val His Gln Leu Tyr Asp Asp Ser Phe Pro Met Glu Ile Arg Gln
 20 25 30

Tyr Leu Ala Gln Trp Leu Glu Lys Gln Asp Trp Glu His Ala Ala Asn
 35 40 45

Asp Val Ser Phe Ala Thr Ile Arg Phe His Asp Leu Leu Ser Gln Leu
 50 55 60

Asp Asp Gln Tyr Ser Arg Phe Ser Leu Glu Asn Asn Phe Leu Leu Gln
 65 70 75 80

His Asn Ile Arg Lys Ser Lys Arg Asn Leu Gln Asp Asn Phe Gln Glu
 85 90 95

Asp Pro Ile Gln Met Ser Met Ile Ile Tyr Ser Cys Leu Lys Glu Glu
 100 105 110

Arg Lys Ile Leu Glu Asn Ala Gln Arg Phe Asn Gln Ala Gln Ser Gly
 115 120 125

Asn Ile Gln Ser Thr Val Met Leu Asp Lys Gln Lys Glu Leu Asp Ser
 130 135 140

Lys Val Arg Asn Val Lys Asp Lys Val Met Cys Ile Glu His Glu Ile
 145 150 155 160

Lys Ser Leu Glu Asp Leu Gln Asp Glu Tyr Asp Phe Lys Cys Lys Thr
 165 170 175

Leu Gln Asn Arg Glu His Glu Thr Asn Gly Val Ala Lys Ser Asp Gln
 180 185 190

Lys Gln Glu Gln Leu Leu Leu Lys Lys Met Tyr Leu Met Leu Asp Asn
 195 200 205

Protein Complexes associated with APP-processing

Lys Arg Lys Glu Val Val His Lys Ile Ile Glu Leu Leu Asn Val Thr
 210 215 220

Glu Leu Thr Gln Asn Ala Leu Ile Asn Asp Glu Leu Val Glu Trp Lys
 225 230 235 240

Arg Arg Gln Gln Ser Ala Cys Ile Gly Gly Pro Pro Asn Ala Cys Leu
 245 250 255

Asp Gln Leu Gln Asn Trp Phe Thr Ile Val Ala Glu Ser Leu Gln Gln
 260 265 270

Val Arg Gln Gln Leu Lys Lys Leu Glu Glu Leu Glu Gln Lys Tyr Thr
 275 280 285

Tyr Glu His Asp Pro Ile Thr Lys Asn Lys Gln Val Leu Trp Asp Arg
 290 295 300

Thr Phe Ser Leu Phe Gln Gln Leu Ile Gln Ser Ser Phe Val Val Glu
 305 310 315 320

Arg Gln Pro Cys Met Pro Thr His Pro Gln Arg Pro Leu Val Leu Lys
 325 330 335

Thr Gly Val Gln Phe Thr Val Lys Leu Arg Leu Leu Val Lys Leu Gln
 340 345 350

Glu Leu Asn Tyr Asn Leu Lys Val Lys Val Leu Phe Asp Lys Asp Val
 355 360 365

Asn Glu Arg Asn Thr Val Lys Gly Phe Arg Lys Phe Asn Ile Leu Gly
 370 375 380

Thr His Thr Lys Val Met Asn Met Glu Glu Ser Thr Asn Gly Ser Leu
 385 390 395 400

Ala Ala Glu Phe Arg His Leu Gln Leu Lys Glu Gln Lys Asn Ala Gly
 405 410 415

Thr Arg Thr Asn Glu Gly Pro Leu Ile Val Thr Glu Glu Leu His Ser
 420 425 430

Leu Ser Phe Glu Thr Gln Leu Cys Gln Pro Gly Leu Val Ile Asp Leu
 435 440 445

Glu Thr Thr Ser Leu Pro Val Val Val Ile Ser Asn Val Ser Gln Leu
 450 455 460

Pro Ser Gly Trp Ala Ser Ile Leu Trp Tyr Asn Met Leu Val Ala Glu
 465 470 475 480

Protein Complexes associated with APP-processing

Pro Arg Asn Leu Ser Phe Phe Leu Thr Pro Pro Cys Ala Arg Trp Ala
485 490 495

Gln Leu Ser Glu Val Leu Ser Trp Gln Phe Ser Ser Val Thr Lys Arg
500 505 510

Gly Leu Asn Val Asp Gln Leu Asn Met Leu Gly Glu Lys Leu Leu Gly
515 520 525

Pro Asn Ala Ser Pro Asp Gly Leu Ile Pro Trp Thr Arg Phe Cys Lys
530 535 540

Glu Asn Ile Asn Asp Lys Asn Phe Pro Phe Trp Leu Trp Ile Glu Ser
545 550 555 560

Ile Leu Glu Leu Ile Lys Lys His Leu Leu Pro Leu Trp Asn Asp Gly
565 570 575

Cys Ile Met Gly Phe Ile Ser Lys Glu Arg Glu Arg Ala Leu Leu Lys
580 585 590

Asp Gln Gln Pro Gly Thr Phe Leu Leu Arg Phe Ser Glu Ser Ser Arg
595 600 605

Glu Gly Ala Ile Thr Phe Thr Trp Val Glu Arg Ser Gln Asn Gly Gly
610 615 620

Glu Pro Asp Phe His Ala Val Glu Pro Tyr Thr Lys Lys Glu Leu Ser
625 630 635 640

Ala Val Thr Phe Pro Asp Ile Ile Arg Asn Tyr Lys Val Met Ala Ala
645 650 655

Glu Asn Ile Pro Glu Asn Pro Leu Lys Tyr Leu Tyr Pro Asn Ile Asp
660 665 670

Lys Asp His Ala Phe Gly Lys Tyr Tyr Ser Arg Pro Lys Glu Ala Pro
675 680 685

Glu Pro Met Glu Leu Asp Gly Pro Lys Gly Thr Gly Tyr Ile Lys Thr
690 695 700

Glu Leu Ile Ser Val Ser Glu Val His Pro Ser Arg Leu Gln Thr Thr
705 710 715 720

Asp Asn Leu Leu Pro Met Ser Pro Glu Glu Phe Asp Glu Val Ser Arg
725 730 735

Ile Val Gly Ser Val Glu Phe Asp Ser Met Met Asn Thr Val
740 745 750

Protein Complexes associated with APP-processing

<210> 203

<211> 550

<212> PRT

<213> Homo sapiens

<400> 203

Met Val Gly Glu Glu Lys Met Ser Leu Arg Asn Arg Leu Ser Lys Ser
 1 5 10 15

Arg Glu Asn Pro Glu Glu Asp Glu Asp Gln Arg Asn Pro Ala Lys Glu
 20 25 30

Ser Leu Glu Thr Pro Ser Asn Gly Arg Ile Asp Ile Lys Gln Leu Ile
 35 40 45

Ala Lys Lys Ile Lys Leu Thr Ala Glu Ala Glu Glu Leu Lys Pro Phe
 50 55 60

Phe Met Lys Glu Val Gly Ser His Phe Asp Asp Phe Val Thr Asn Leu
 65 70 75 80

Ile Glu Lys Ser Ala Ser Leu Asp Asn Gly Gly Cys Ala Leu Thr Thr
 85 90 95

Phe Ser Val Leu Glu Gly Glu Lys Asn Asn His Arg Ala Lys Asp Leu
 100 105 110

Arg Ala Pro Pro Glu Gln Gly Lys Ile Phe Ile Ala Arg Arg Ser Leu
 115 120 125

Leu Asp Glu Leu Leu Glu Val Asp His Ile Arg Thr Ile Tyr His Met
 130 135 140

Phe Ile Ala Leu Leu Ile Leu Phe Ile Leu Ser Thr Leu Val Val Asp
 145 150 155 160

Tyr Ile Asp Glu Gly Arg Leu Val Leu Glu Phe Ser Leu Leu Ser Tyr
 165 170 175

Ala Phe Gly Lys Phe Pro Thr Val Val Trp Thr Trp Trp Ile Met Phe
 180 185 190

Leu Ser Thr Phe Ser Val Pro Tyr Phe Leu Phe Gln His Trp Ala Thr
 195 200 205

Gly Tyr Ser Lys Ser Ser His Pro Leu Ile Arg Ser Leu Phe His Gly
 210 215 220

Protein Complexes associated with APP-processing

Phe Leu Phe Met Ile Phe Gln Ile Gly Val Leu Gly Phe Gly Pro Thr
 225 230 235 240

Tyr Val Val Leu Ala Tyr Thr Leu Pro Pro Ala Ser Arg Phe Ile Ile
 245 250 255

Ile Phe Glu Gln Ile Arg Phe Val Met Lys Ala His Ser Phe Val Arg
 260 265 270

Glu Asn Val Pro Arg Val Leu Asn Ser Ala Lys Glu Lys Ser Ser Thr
 275 280 285

Val Pro Ile Pro Thr Val Asn Gln Tyr Leu Tyr Phe Leu Phe Ala Pro
 290 295 300

Thr Leu Ile Tyr Arg Asp Ser Tyr Pro Arg Asn Pro Thr Val Arg Trp
 305 310 315 320

Gly Tyr Val Ala Met Lys Phe Ala Gln Val Phe Gly Cys Phe Phe Tyr
 325 330 335

Val Tyr Tyr Ile Phe Glu Arg Leu Cys Ala Pro Leu Phe Arg Asn Ile
 340 345 350

Lys Gln Glu Pro Phe Ser Ala Arg Val Leu Val Leu Cys Val Phe Asn
 355 360 365

Ser Ile Leu Pro Gly Val Leu Ile Leu Phe Leu Thr Phe Phe Ala Phe
 370 375 380

Leu His Cys Trp Leu Asn Ala Phe Ala Glu Met Leu Arg Phe Gly Asp
 385 390 395 400

Arg Met Phe Tyr Lys Asp Trp Trp Asn Ser Thr Ser Tyr Ser Asn Tyr
 405 410 415

Tyr Arg Thr Trp Asn Val Val Val His Asp Trp Leu Tyr Tyr Tyr Ala
 420 425 430

Tyr Lys Asp Phe Leu Trp Phe Phe Ser Lys Arg Phe Lys Ser Ala Ala
 435 440 445

Met Leu Ala Val Phe Ala Val Ser Ala Val Val His Glu Tyr Ala Leu
 450 455 460

Ala Val Cys Leu Ser Phe Phe Tyr Pro Val Leu Phe Val Leu Phe Met
 465 470 475 480

Phe Phe Gly Met Ala Phe Asn Phe Ile Val Asn Asp Ser Arg Lys Lys
 485 490 495

Protein Complexes associated with APP-processing
 Pro Ile Trp Asn Val Leu Met Trp Thr Ser Leu Phe Leu Gly Asn Gly
 500 505 510

Val Leu Leu Cys Phe Tyr Ser Gln Glu Trp Tyr Ala Arg Arg His Cys
 515 520 525

Pro Leu Lys Asn Pro Thr Phe Leu Asp Tyr Val Arg Pro Arg Ser Trp
 530 535 540

Thr Cys Arg Tyr Val Phe
 545 550

<210> 204

<211> 2861

<212> PRT

<213> Homo sapiens

<400> 204

Met Lys Ala Met Asp Val Leu Pro Ile Leu Lys Glu Lys Val Ala Tyr
 1 5 10 15

Leu Ser Gly Gly Arg Asp Lys Arg Gly Gly Pro Ile Leu Thr Phe Pro
 20 25 30

Ala Arg Ser Asn His Asp Arg Ile Arg Gln Glu Asp Leu Arg Arg Leu
 35 40 45

Ile Ser Tyr Leu Ala Cys Ile Pro Ser Glu Glu Val Cys Lys Arg Gly
 50 55 60

Phe Thr Val Ile Val Asp Met Arg Gly Ser Lys Trp Asp Ser Ile Lys
 65 70 75 80

Pro Leu Leu Lys Ile Leu Gln Glu Ser Phe Pro Cys Cys Ile His Val
 85 90 95

Ala Leu Ile Ile Lys Pro Asp Asn Phe Trp Gln Lys Gln Arg Thr Asn
 100 105 110

Phe Gly Ser Ser Lys Phe Glu Phe Glu Thr Asn Met Val Ser Leu Glu
 115 120 125

Gly Leu Thr Lys Val Val Asp Pro Ser Gln Leu Thr Pro Glu Phe Asp
 130 135 140

Gly Cys Leu Glu Tyr Asn His Glu Glu Trp Ile Glu Ile Arg Val Ala
 145 150 155 160

Protein Complexes associated with APP-processing

Phe Glu Asp Tyr Ile Ser Asn Ala Thr His Met Leu Ser Arg Leu Glu
165 170 175

Glu Leu Gln Asp Ile Leu Ala Lys Lys Glu Leu Pro Gln Asp Leu Glu
180 185 190

Gly Ala Arg Asn Met Ile Glu Glu His Ser Gln Leu Lys Lys Lys Val
195 200 205

Ile Lys Ala Pro Ile Glu Asp Leu Asp Leu Glu Gly Gln Lys Leu Leu
210 215 220

Gln Arg Ile Gln Ser Ser Glu Ser Phe Pro Lys Lys Asn Ser Gly Ser
225 230 235 240

Gly Asn Ala Asp Leu Gln Asn Leu Leu Pro Lys Val Ser Thr Met Leu
245 250 255

Asp Arg Leu His Ser Thr Arg Gln His Leu His Gln Met Trp His Val
260 265 270

Arg Lys Leu Lys Leu Asp Gln Cys Phe Gln Leu Arg Leu Phe Glu Gln
275 280 285

Asp Ala Glu Lys Met Phe Asp Trp Ile Thr His Asn Lys Gly Leu Phe
290 295 300

Leu Asn Ser Tyr Thr Glu Ile Gly Thr Ser His Pro His Ala Met Glu
305 310 315 320

Leu Gln Thr Gln His Asn His Phe Ala Met Asn Cys Met Asn Val Tyr
325 330 335

Val Asn Ile Asn Arg Ile Met Ser Val Ala Asn Arg Leu Val Glu Ser
340 345 350

Gly His Tyr Ala Ser Gln Gln Ile Arg Gln Ile Ala Ser Gln Leu Glu
355 360 365

Gln Glu Trp Lys Ala Phe Ala Ala Ala Leu Asp Glu Arg Ser Thr Leu
370 375 380

Leu Asp Met Ser Ser Ile Phe His Gln Lys Ala Glu Lys Tyr Met Ser
385 390 395 400

Asn Val Asp Ser Trp Cys Lys Ala Cys Gly Glu Val Asp Leu Pro Ser
405 410 415

Glu Leu Gln Asp Leu Glu Asp Ala Ile His His His Gln Gly Ile Tyr
420 425 430

Protein Complexes associated with APP-processing
 Glu His Ile Thr Leu Ala Tyr Ser Glu Val Ser Gln Asp Gly Lys Ser
 435 440 445

Leu Leu Asp Lys Leu Gln Arg Pro Leu Thr Pro Gly Ser Ser Asp Ser
 450 455 460

Leu Thr Ala Ser Ala Asn Tyr Ser Lys Ala Val His His Val Leu Asp
 465 470 475 480

Val Ile His Glu Val Leu His His Gln Arg His Val Arg Thr Ile Trp
 485 490 495

Gln His Arg Lys Val Arg Leu His Gln Arg Leu Gln Leu Cys Val Phe
 500 505 510

Gln Gln Glu Val Gln Gln Val Leu Asp Trp Ile Glu Asn His Gly Glu
 515 520 525

Ala Phe Leu Ser Lys His Thr Gly Val Gly Lys Ser Leu His Arg Ala
 530 535 540

Arg Ala Leu Gln Lys Arg His Glu Asp Phe Glu Glu Val Ala Gln Asn
 545 550 555 560

Thr Tyr Thr Asn Ala Asp Lys Leu Leu Glu Ala Ala Glu Gln Leu Ala
 565 570 575

Gln Thr Gly Glu Cys Asp Pro Glu Glu Ile Tyr Gln Ala Ala His Gln
 580 585 590

Leu Glu Asp Arg Ile Gln Asp Phe Val Arg Arg Val Glu Gln Arg Lys
 595 600 605

Ile Leu Leu Asp Met Ser Val Ser Phe His Thr His Val Lys Glu Leu
 610 615 620

Trp Thr Trp Leu Glu Glu Leu Gln Lys Glu Leu Leu Asp Asp Val Tyr
 625 630 635 640

Ala Glu Ser Val Glu Ala Val Gln Asp Leu Ile Lys Arg Phe Gly Gln
 645 650 655

Gln Gln Gln Thr Thr Leu Gln Val Thr Val Asn Val Ile Lys Glu Gly
 660 665 670

Glu Asp Leu Ile Gln Gln Leu Arg Asp Ser Ala Ile Ser Ser Asn Lys
 675 680 685

Thr Pro His Asn Ser Ser Ile Asn His Ile Glu Thr Val Leu Gln Gln
 690 695 700

Protein Complexes associated with APP-processing

Leu Asp Glu Ala Gln Ser Gln Met Glu Glu Leu Phe Gln Glu Arg Lys
 705 710 715 720
 Ile Lys Leu Glu Leu Phe Leu His Val Arg Ile Phe Glu Arg Asp Ala
 725 730 735
 Ile Asp Ile Ile Ser Asp Leu Glu Ser Trp Asn Asp Glu Leu Ser Gln
 740 745 750
 Gln Met Asn Asp Phe Asp Thr Glu Asp Leu Thr Ile Ala Glu Gln Arg
 755 760 765
 Leu Gln His His Ala Asp Lys Ala Leu Thr Met Asn Asn Leu Thr Phe
 770 775 780
 Asp Val Ile His Gln Gly Gln Asp Leu Leu Gln Tyr Val Asn Glu Val
 785 790 795 800
 Gln Ala Ser Gly Val Glu Leu Leu Cys Asp Arg Asp Val Asp Met Ala
 805 810 815
 Thr Arg Val Gln Asp Leu Leu Glu Phe Leu His Glu Lys Gln Gln Glu
 820 825 830
 Leu Asp Leu Ala Ala Glu Gln His Arg Lys His Leu Glu Gln Cys Val
 835 840 845
 Gln Leu Arg His Leu Gln Ala Glu Val Lys Gln Val Leu Gly Trp Ile
 850 855 860
 Arg Asn Gly Glu Ser Met Leu Asn Ala Gly Leu Ile Thr Ala Ser Ser
 865 870 875 880
 Leu Gln Glu Ala Glu Gln Leu Gln Arg Glu His Glu Gln Phe Gln His
 885 890 895
 Ala Ile Glu Lys Thr His Gln Ser Ala Leu Gln Val Gln Gln Lys Ala
 900 905 910
 Glu Ala Met Leu Gln Ala Asn His Tyr Asp Met Asp Met Ile Arg Asp
 915 920 925
 Cys Ala Glu Lys Val Ala Ser His Trp Gln Gln Leu Met Leu Lys Met
 930 935 940
 Glu Asp Arg Leu Lys Leu Val Asn Ala Ser Val Ala Phe Tyr Lys Thr
 945 950 955 960
 Ser Glu Gln Val Cys Ser Val Leu Glu Ser Leu Glu Gln Glu Tyr Lys
 965 970 975

Protein Complexes associated with APP-processing
 Arg Glu Glu Asp Trp Cys Gly Gly Ala Asp Lys Leu Gly Pro Asn Ser
 980 985 990

Glu Thr Asp His Val Thr Pro Met Ile Ser Lys His Leu Glu Gln Lys
 995 1000 1005

Glu Ala Phe Leu Lys Ala Cys Thr Leu Ala Arg Arg Asn Ala Asp
 1010 1015 1020

Val Phe Leu Lys Tyr Leu His Arg Asn Ser Val Asn Met Pro Gly
 1025 1030 1035

Met Val Thr His Ile Lys Ala Pro Glu Gln Gln Val Lys Asn Ile
 1040 1045 1050

Leu Asn Glu Leu Phe Gln Arg Glu Asn Arg Val Leu His Tyr Trp
 1055 1060 1065

Thr Met Arg Lys Arg Arg Leu Asp Gln Cys Gln Gln Tyr Val Val
 1070 1075 1080

Phe Glu Arg Ser Ala Lys Gln Ala Leu Glu Trp Ile His Asp Asn
 1085 1090 1095

Gly Glu Phe Tyr Leu Ser Thr His Thr Ser Thr Gly Ser Ser Ile
 1100 1105 1110

Gln His Thr Gln Glu Leu Leu Lys Glu His Glu Glu Phe Gln Ile
 1115 1120 1125

Thr Ala Lys Gln Thr Lys Glu Arg Val Lys Leu Leu Ile Gln Leu
 1130 1135 1140

Ala Asp Gly Phe Cys Glu Lys Gly His Ala His Ala Ala Glu Ile
 1145 1150 1155

Lys Lys Cys Val Thr Ala Val Asp Lys Arg Tyr Arg Asp Phe Ser
 1160 1165 1170

Leu Arg Met Glu Lys Tyr Arg Thr Ser Leu Glu Lys Ala Leu Gly
 1175 1180 1185

Ile Ser Ser Asp Ser Asn Lys Ser Ser Lys Ser Leu Gln Leu Asp
 1190 1195 1200

Ile Ile Pro Ala Ser Ile Pro Gly Ser Glu Val Lys Leu Arg Asp
 1205 1210 1215

Ala Ala His Glu Leu Asn Glu Glu Lys Arg Lys Ser Ala Arg Arg
 1220 1225 1230

Protein Complexes associated with APP-processing

Lys Glu Phe Ile Met Ala Glu Leu Ile Gln Thr Glu Lys Ala Tyr
 1235 1240 1245

Val Arg Asp Leu Arg Glu Cys Met Asp Thr Tyr Leu Trp Glu Met
 1250 1255 1260

Thr Ser Gly Val Glu Glu Ile Pro Pro Gly Ile Val Asn Lys Glu
 1265 1270 1275

Leu Ile Ile Phe Gly Asn Met Gln Glu Ile Tyr Glu Phe His Asn
 1280 1285 1290

Asn Ile Phe Leu Lys Glu Leu Glu Lys Tyr Glu Gln Leu Pro Glu
 1295 1300 1305

Asp Val Gly His Cys Phe Val Thr Trp Ala Asp Lys Phe Gln Met
 1310 1315 1320

Tyr Val Thr Tyr Cys Lys Asn Lys Pro Asp Ser Thr Gln Leu Ile
 1325 1330 1335

Leu Glu His Ala Gly Ser Tyr Phe Asp Glu Ile Gln Gln Arg His
 1340 1345 1350

Gly Leu Ala Asn Ser Ile Ser Ser Tyr Leu Ile Lys Pro Val Gln
 1355 1360 1365

Arg Ile Thr Lys Tyr Gln Leu Leu Leu Lys Glu Leu Leu Thr Cys
 1370 1375 1380

Cys Glu Glu Gly Lys Gly Glu Ile Lys Asp Gly Leu Glu Val Met
 1385 1390 1395

Leu Ser Val Pro Lys Arg Ala Asn Asp Ala Met His Leu Ser Met
 1400 1405 1410

Leu Glu Gly Phe Asp Glu Asn Ile Glu Ser Gln Gly Glu Leu Ile
 1415 1420 1425

Leu Gln Glu Ser Phe Gln Val Trp Asp Pro Lys Thr Leu Ile Arg
 1430 1435 1440

Lys Gly Arg Glu Arg His Leu Phe Leu Phe Glu Met Ser Leu Val
 1445 1450 1455

Phe Ser Lys Glu Val Lys Asp Ser Ser Gly Arg Ser Lys Tyr Leu
 1460 1465 1470

Tyr Lys Ser Lys Leu Phe Thr Ser Glu Leu Gly Val Thr Glu His
 1475 1480 1485

Protein Complexes associated with APP-processing

Val	Glu	Gly	Asp	Pro	Cys	Lys	Phe	Ala	Leu	Trp	Val	Gly	Arg	Thr
1490						1495					1500			
Pro	Thr	Ser	Asp	Asn	Lys	Ile	Val	Leu	Lys	Ala	Ser	Ser	Ile	Glu
1505						1510					1515			
Asn	Lys	Gln	Asp	Trp	Ile	Lys	His	Ile	Arg	Glu	Val	Ile	Gln	Glu
1520						1525					1530			
Arg	Thr	Ile	His	Leu	Lys	Gly	Ala	Leu	Lys	Glu	Pro	Ile	His	Ile
1535						1540					1545			
Pro	Lys	Thr	Ala	Pro	Ala	Thr	Arg	Gln	Lys	Gly	Arg	Arg	Asp	Gly
1550						1555					1560			
Glu	Asp	Leu	Asp	Ser	Gln	Gly	Asp	Gly	Ser	Ser	Gln	Pro	Asp	Thr
1565						1570					1575			
Ile	Ser	Ile	Ala	Ser	Arg	Thr	Ser	Gln	Asn	Thr	Leu	Asp	Ser	Asp
1580						1585					1590			
Lys	Leu	Ser	Gly	Gly	Cys	Glu	Leu	Thr	Val	Val	Ile	His	Asp	Phe
1595						1600					1605			
Thr	Ala	Cys	Asn	Ser	Asn	Glu	Leu	Thr	Ile	Arg	Arg	Gly	Gln	Thr
1610						1615					1620			
Val	Glu	Val	Leu	Glu	Arg	Pro	His	Asp	Lys	Pro	Asp	Trp	Cys	Leu
1625						1630					1635			
Val	Arg	Thr	Thr	Asp	Arg	Ser	Pro	Ala	Ala	Glu	Gly	Leu	Val	Pro
1640						1645					1650			
Cys	Gly	Ser	Leu	Cys	Ile	Ala	His	Ser	Arg	Ser	Ser	Met	Glu	Met
1655						1660					1665			
Glu	Gly	Ile	Phe	Asn	His	Lys	Asp	Ser	Leu	Ser	Val	Ser	Ser	Asn
1670						1675					1680			
Asp	Ala	Ser	Pro	Pro	Ala	Ser	Val	Ala	Ser	Leu	Gln	Pro	His	Met
1685						1690					1695			
Ile	Gly	Ala	Gln	Ser	Ser	Pro	Gly	Pro	Lys	Arg	Pro	Gly	Asn	Thr
1700						1705					1710			
Leu	Arg	Lys	Trp	Leu	Thr	Ser	Pro	Val	Arg	Arg	Leu	Ser	Ser	Gly
1715						1720					1725			
Lys	Ala	Asp	Gly	His	Val	Lys	Lys	Leu	Ala	His	Lys	His	Lys	Lys
1730						1735					1740			

Protein Complexes associated with APP-processing

Ser Arg Glu Val Arg Lys Ser Ala Asp Ala Gly Ser Gln Lys Asp
 1745 1750 1755

Ser Asp Asp Ser Ala Ala Thr Pro Gln Asp Glu Thr Val Glu Glu
 1760 1765 1770

Arg Gly Arg Asn Glu Gly Leu Ser Ser Gly Thr Leu Ser Lys Ser
 1775 1780 1785

Ser Ser Ser Gly Met Gln Ser Cys Gly Glu Glu Glu Gly Glu Glu
 1790 1795 1800

Gly Ala Asp Ala Val Pro Leu Pro Pro Pro Met Ala Ile Gln Gln
 1805 1810 1815

His Ser Leu Leu Gln Pro Asp Ser Gln Asp Asp Lys Ala Ser Ser
 1820 1825 1830

Arg Leu Leu Val Arg Pro Thr Ser Ser Glu Thr Pro Ser Ala Ala
 1835 1840 1845

Glu Leu Val Ser Ala Ile Glu Glu Leu Val Lys Ser Lys Met Ala
 1850 1855 1860

Leu Glu Asp Arg Pro Ser Ser Leu Leu Val Asp Gln Gly Asp Ser
 1865 1870 1875

Ser Ser Pro Ser Phe Asn Pro Ser Asp Asn Ser Leu Leu Ser Ser
 1880 1885 1890

Ser Ser Pro Ile Asp Glu Met Glu Glu Arg Lys Ser Ser Ser Leu
 1895 1900 1905

Lys Arg Arg His Tyr Val Leu Gln Glu Leu Val Glu Thr Glu Arg
 1910 1915 1920

Asp Tyr Val Arg Asp Leu Gly Tyr Val Val Glu Gly Tyr Met Ala
 1925 1930 1935

Leu Met Lys Glu Asp Gly Val Pro Asp Asp Met Lys Gly Lys Asp
 1940 1945 1950

Lys Ile Val Phe Gly Asn Ile His Gln Ile Tyr Asp Trp His Arg
 1955 1960 1965

Asp Phe Phe Leu Gly Glu Leu Glu Lys Cys Leu Glu Asp Pro Glu
 1970 1975 1980

Lys Leu Gly Ser Leu Phe Val Lys His Glu Arg Arg Leu His Met
 1985 1990 1995

Protein Complexes associated with APP-processing
 Tyr Ile Ala Tyr Cys Gln Asn Lys Pro Lys Ser Glu His Ile Val
 2000 2005 2010

Ser Glu Tyr Ile Asp Thr Phe Phe Glu Asp Leu Lys Gln Arg Leu
 2015 2020 2025

Gly His Arg Leu Gln Leu Thr Asp Leu Leu Ile Lys Pro Val Gln
 2030 2035 2040

Arg Ile Met Lys Tyr Gln Leu Leu Leu Lys Asp Phe Leu Lys Tyr
 2045 2050 2055

Ser Lys Lys Ala Ser Leu Asp Thr Ser Glu Leu Glu Arg Ala Val
 2060 2065 2070

Glu Val Met Cys Ile Val Pro Arg Arg Cys Asn Asp Met Met Asn
 2075 2080 2085

Val Gly Arg Leu Gln Gly Phe Asp Gly Lys Ile Val Ala Gln Gly
 2090 2095 2100

Lys Leu Leu Leu Gln Asp Thr Phe Leu Val Thr Asp Gln Asp Ala
 2105 2110 2115

Gly Leu Leu Pro Arg Cys Arg Glu Arg Arg Ile Phe Leu Phe Glu
 2120 2125 2130

Gln Ile Val Ile Phe Ser Glu Pro Leu Asp Lys Lys Lys Gly Phe
 2135 2140 2145

Ser Met Pro Gly Phe Leu Phe Lys Asn Ser Ile Lys Val Ser Cys
 2150 2155 2160

Leu Cys Leu Glu Glu Asn Val Glu Asn Asp Pro Cys Lys Phe Ala
 2165 2170 2175

Leu Thr Ser Arg Thr Gly Asp Val Val Glu Thr Phe Ile Leu His
 2180 2185 2190

Ser Ser Ser Pro Ser Val Arg Gln Thr Trp Ile His Glu Ile Asn
 2195 2200 2205

Gln Ile Leu Glu Asn Gln Arg Asn Phe Leu Asn Ala Leu Thr Ser
 2210 2215 2220

Pro Ile Glu Tyr Gln Arg Asn His Ser Gly Gly Gly Gly Gly Gly
 2225 2230 2235

Gly Ser Gly Ala Ala Ala Gly Val Gly Ala Ala Ala Ala Ala Gly
 2240 2245 2250

Protein Complexes associated with APP-processing

Pro 2255 Val Ala Ala Ala Thr Val Ala Ala Pro 2265 Ala Ala Ala

Ala 2270 Pro Pro Ala Arg Ala 2275 Gly Ala Gly Pro Pro 2280 Gly Ser Pro

Ser 2285 Leu Ser Asp Thr Thr Pro 2290 Pro Cys Trp Ser Pro 2295 Leu Gln Pro

Arg 2300 Ala Arg Gln Arg Gln Thr 2305 Arg Cys Gln Ser Glu 2310 Ser Ser Ser

Ser 2315 Ser Asn Ile Ser Thr Met 2320 Leu Val Thr His Asp 2325 Tyr Thr Ala

Val 2330 Lys Glu Asp Glu Ile Asn 2335 Val Tyr Gln Gly Glu 2340 Val Val Gln

Ile 2345 Leu Ala Ser Asn Gln Gln 2350 Asn Met Phe Leu Val 2355 Phe Arg Ala

Ala 2360 Thr Asp Gln Cys Pro Ala 2365 Ala Glu Gly Trp Ile 2370 Pro Gly Phe

Val 2375 Leu Gly His Thr Ser Ala 2380 Val Ile Val Glu Asn 2385 Pro Asp Gly

Thr 2390 Leu Lys Lys Ser Thr Ser 2395 Trp His Thr Ala Leu 2400 Arg Leu Arg

Lys 2405 Lys Ser Glu Lys Lys Asp 2410 Lys Asp Gly Lys Arg 2415 Glu Gly Lys

Leu 2420 Glu Asn Gly Tyr Arg Lys 2425 Ser Arg Glu Gly Leu 2430 Ser Asn Lys

Val 2435 Ser Val Lys Leu Leu Asn 2440 Pro Asn Tyr Ile Tyr 2445 Asp Val Pro

Pro 2450 Glu Phe Val Ile Pro Leu 2455 Ser Glu Val Thr Cys 2460 Glu Thr Gly

Glu 2465 Thr Val Val Leu Arg Cys 2470 Arg Val Cys Gly Arg 2475 Pro Lys Ala

Ser 2480 Ile Thr Trp Lys Gly Pro 2485 Glu His Asn Thr Leu 2490 Asn Asn Asp

Gly 2495 His Tyr Ser Ile Ser Tyr 2500 Ser Asp Leu Gly Glu 2505 Ala Thr Leu

Protein Complexes associated with APP-processing

Lys Ile Val Gly Val Thr Thr Glu Asp Asp Gly Ile Tyr Thr Cys
 2510 2515 2520

Ile Ala Val Asn Asp Met Gly Ser Ala Ser Ser Ser Ala Ser Leu
 2525 2530 2535

Arg Val Leu Gly Pro Gly Met Asp Gly Ile Met Val Thr Trp Lys
 2540 2545 2550

Asp Asn Phe Asp Ser Phe Tyr Ser Glu Val Ala Glu Leu Gly Arg
 2555 2560 2565

Gly Arg Phe Ser Val Val Lys Lys Cys Asp Gln Lys Gly Thr Lys
 2570 2575 2580

Arg Ala Val Ala Thr Lys Phe Val Asn Lys Lys Leu Met Lys Arg
 2585 2590 2595

Asp Gln Val Thr His Glu Leu Gly Ile Leu Gln Ser Leu Gln His
 2600 2605 2610

Pro Leu Leu Val Gly Leu Leu Asp Thr Phe Glu Thr Pro Thr Ser
 2615 2620 2625

Tyr Ile Leu Val Leu Glu Met Ala Asp Gln Gly Arg Leu Leu Asp
 2630 2635 2640

Cys Val Val Arg Trp Gly Ser Leu Thr Glu Gly Lys Ile Arg Ala
 2645 2650 2655

His Leu Gly Glu Val Leu Glu Ala Val Arg Tyr Leu His Asn Cys
 2660 2665 2670

Arg Ile Ala His Leu Asp Leu Lys Pro Glu Asn Ile Leu Val Asp
 2675 2680 2685

Glu Ser Leu Ala Lys Pro Thr Ile Lys Leu Ala Asp Phe Gly Asp
 2690 2695 2700

Ala Val Gln Leu Asn Thr Thr Tyr Tyr Ile His Gln Leu Leu Gly
 2705 2710 2715

Asn Pro Glu Phe Ala Ala Pro Glu Ile Ile Leu Gly Asn Pro Val
 2720 2725 2730

Ser Leu Thr Ser Asp Thr Trp Ser Val Gly Val Leu Thr Tyr Val
 2735 2740 2745

Leu Leu Ser Gly Val Ser Pro Phe Leu Asp Asp Ser Val Glu Glu
 2750 2755 2760

Protein Complexes associated with APP-processing

Thr Cys Leu Asn Ile Cys Arg Leu Asp Phe Ser Phe Pro Asp Asp
 2765 2770 2775

Tyr Phe Lys Gly Val Ser Gln Lys Ala Lys Glu Phe Val Cys Phe
 2780 2785 2790

Leu Leu Gln Glu Asp Pro Ala Lys Arg Pro Ser Ala Ala Leu Ala
 2795 2800 2805

Leu Gln Glu Gln Trp Leu Gln Ala Gly Asn Gly Arg Ser Thr Gly
 2810 2815 2820

Val Leu Asp Thr Ser Arg Leu Thr Ser Phe Ile Glu Arg Arg Lys
 2825 2830 2835

His Gln Asn Asp Val Arg Pro Ile Arg Ser Ile Lys Asn Phe Leu
 2840 2845 2850

Gln Ser Arg Leu Leu Pro Arg Val
 2855 2860

<210> 205

<211> 350

<212> PRT

<213> Homo sapiens

<400> 205

Met Ala Val Phe Val Val Leu Leu Ala Leu Val Ala Gly Val Leu Gly
 1 5 10 15

Asn Glu Phe Ser Ile Leu Lys Ser Pro Gly Ser Val Val Phe Arg Asn
 20 25 30

Gly Asn Trp Pro Ile Pro Gly Glu Arg Ile Pro Asp Val Ala Ala Leu
 35 40 45

Ser Met Gly Phe Ser Val Lys Glu Asp Leu Ser Trp Pro Gly Leu Ala
 50 55 60

Val Gly Asn Leu Phe His Arg Pro Arg Ala Thr Val Met Val Met Val
 65 70 75 80

Lys Gly Val Asn Lys Leu Ala Leu Pro Pro Gly Ser Val Ile Ser Tyr
 85 90 95

Pro Leu Glu Asn Ala Val Pro Phe Ser Leu Asp Ser Val Ala Asn Ser
 100 105 110

Protein Complexes associated with APP-processing
 Ile His Ser Leu Phe Ser Glu Glu Thr Pro Val Val Leu Gln Leu Ala
 115 120 125

Pro Ser Glu Glu Arg Val Tyr Met Val Gly Lys Ala Asn Ser Val Phe
 130 135 140

Glu Asp Leu Ser Val Thr Leu Arg Gln Leu Arg Asn Arg Leu Phe Gln
 145 150 155 160

Glu Asn Ser Val Leu Ser Ser Leu Pro Leu Asn Ser Leu Ser Arg Asn
 165 170 175

Asn Glu Val Asp Leu Leu Phe Leu Ser Glu Leu Gln Val Leu His Asp
 180 185 190

Ile Ser Ser Leu Leu Ser Arg His Lys His Leu Ala Lys Asp His Ser
 195 200 205

Pro Asp Leu Tyr Ser Leu Glu Leu Ala Gly Leu Asp Glu Ile Gly Lys
 210 215 220

Arg Tyr Gly Glu Asp Ser Glu Gln Phe Arg Asp Ala Ser Lys Ile Leu
 225 230 235 240

Val Asp Ala Leu Gln Lys Phe Ala Asp Asp Met Tyr Ser Leu Tyr Gly
 245 250 255

Gly Asn Ala Val Val Glu Leu Val Thr Val Lys Ser Phe Asp Thr Ser
 260 265 270

Leu Ile Arg Lys Thr Arg Thr Ile Leu Glu Ala Lys Arg Ala Lys Asn
 275 280 285

Pro Ala Ser Pro Tyr Asn Leu Ala Tyr Lys Tyr Asn Phe Glu Tyr Ser
 290 295 300

Val Val Phe Asn Met Val Leu Trp Ile Met Ile Ala Leu Ala Leu Ala
 305 310 315 320

Val Ile Ile Thr Ser Tyr Asn Ile Trp Asn Met Asp Pro Gly Tyr Asp
 325 330 335

Ser Ile Ile Tyr Arg Met Thr Asn Gln Lys Ile Arg Met Asp
 340 345 350

<210> 206

<211> 180

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 206

Met Asn Thr Val Leu Ser Arg Ala Asn Ser Leu Phe Ala Phe Ser Leu
 1 5 10 15

Ser Val Met Ala Ala Leu Thr Phe Gly Cys Phe Ile Thr Thr Ala Phe
 20 25 30

Lys Asp Arg Ser Val Pro Val Arg Leu His Val Ser Arg Ile Met Leu
 35 40 45

Lys Asn Val Glu Asp Phe Thr Gly Pro Arg Glu Arg Ser Asp Leu Gly
 50 55 60

Phe Ile Thr Ser Asp Ile Thr Ala Asp Leu Glu Asn Ile Phe Asp Trp
 65 70 75 80

Asn Val Lys Gln Leu Phe Leu Tyr Leu Ser Ala Glu Tyr Ser Thr Lys
 85 90 95

Asn Asn Ala Leu Asn Gln Val Val Leu Trp Asp Lys Ile Val Leu Arg
 100 105 110

Gly Asp Asn Pro Lys Leu Leu Leu Lys Asp Met Lys Thr Lys Tyr Phe
 115 120 125

Phe Phe Asp Asp Gly Asn Gly Leu Lys Gly Asn Arg Asn Val Thr Leu
 130 135 140

Thr Leu Ser Trp Asn Val Val Pro Asn Ala Gly Ile Leu Pro Leu Val
 145 150 155 160

Thr Gly Ser Gly His Val Ser Val Pro Phe Pro Asp Thr Tyr Glu Ile
 165 170 175

Thr Lys Ser Tyr
 180

<210> 207

<211> 670

<212> PRT

<213> Homo sapiens

<400> 207

Met Gly Glu Pro Ala Gly Val Ala Gly Thr Met Glu Ser Pro Phe Ser
 1 5 10 15

Protein Complexes associated with APP-processing

Pro Gly Leu Phe His Arg Leu Asp Glu Asp Trp Asp Ser Ala Leu Phe
 20 25 30

Ala Glu Leu Gly Tyr Phe Thr Asp Thr Asp Glu Leu Gln Leu Glu Ala
 35 40 45

Ala Asn Glu Thr Tyr Glu Asn Asn Phe Asp Asn Leu Asp Phe Asp Leu
 50 55 60

Asp Leu Leu Pro Trp Glu Ser Asp Ile Trp Asp Ile Asn Asn Gln Ile
 65 70 75 80

Cys Thr Val Lys Asp Ile Lys Ala Glu Pro Gln Pro Leu Ser Pro Ala
 85 90 95

Ser ser Ser Tyr Ser Val Ser Ser Pro Arg Ser Val Asp Ser Tyr Ser
 100 105 110

Ser Thr Gln His Val Pro Glu Glu Leu Asp Leu Ser Ser Ser Ser Gln
 115 120 125

Met Ser Pro Leu Ser Leu Tyr Gly Glu Asn Ser Asn Ser Leu Ser Ser
 130 135 140

Pro Glu Pro Leu Lys Glu Asp Lys Pro Val Thr Gly Ser Arg Asn Lys
 145 150 155 160

Thr Glu Asn Gly Leu Thr Pro Lys Lys Lys Ile Gln Val Asn Ser Lys
 165 170 175

Pro Ser Ile Gln Pro Lys Pro Leu Leu Leu Pro Ala Ala Pro Lys Thr
 180 185 190

Gln Thr Asn Ser Ser Val Pro Ala Lys Thr Ile Ile Ile Gln Thr Val
 195 200 205

Pro Thr Leu Met Pro Leu Ala Lys Gln Gln Pro Ile Ile Ser Leu Gln
 210 215 220

Pro Ala Pro Thr Lys Gly Gln Thr Val Leu Leu Ser Gln Pro Thr Val
 225 230 235 240

Val Gln Leu Gln Ala Pro Gly Val Leu Pro Ser Ala Gln Pro Val Leu
 245 250 255

Ala Val Ala Gly Gly Val Thr Gln Leu Pro Asn His Val Val Asn Val
 260 265 270

Val Pro Ala Pro Ser Ala Asn Ser Pro Val Asn Gly Lys Leu Ser Val
 275 280 285

Protein Complexes associated with APP-processing

Thr Lys Pro Val Leu Gln Ser Thr Met Arg Asn Val Gly Ser Asp Ile
 290 295 300

Ala Val Leu Arg Arg Gln Gln Arg Met Ile Lys Asn Arg Glu Ser Ala
 305 310 315 320

Cys Gln Ser Arg Lys Lys Lys Lys Glu Tyr Met Leu Gly Leu Glu Ala
 325 330 335

Arg Leu Lys Ala Ala Leu Ser Glu Asn Glu Gln Leu Lys Lys Glu Asn
 340 345 350

Gly Thr Leu Lys Arg Gln Leu Asp Glu Val Val Ser Glu Asn Gln Arg
 355 360 365

Leu Lys Val Pro Ser Pro Lys Arg Arg Val Val Cys Val Met Ile Val
 370 375 380

Leu Ala Phe Ile Ile Leu Asn Tyr Gly Pro Met Ser Met Leu Glu Gln
 385 390 395 400

Asp Ser Arg Arg Met Asn Pro Ser Val Gly Pro Ala Asn Gln Arg Arg
 405 410 415

His Leu Leu Gly Phe Ser Ala Lys Glu Ala Gln Asp Thr Ser Asp Gly
 420 425 430

Ile Ile Gln Lys Asn Ser Tyr Arg Tyr Asp His Ser Val Ser Asn Asp
 435 440 445

Lys Ala Leu Met Val Leu Thr Glu Glu Pro Leu Leu Tyr Ile Pro Pro
 450 455 460

Pro Pro Cys Gln Pro Leu Ile Asn Thr Thr Glu Ser Leu Arg Leu Asn
 465 470 475 480

His Glu Leu Arg Gly Trp Val His Arg His Glu Val Glu Arg Thr Lys
 485 490 495

Ser Arg Arg Met Thr Asn Asn Gln Gln Lys Thr Arg Ile Leu Gln Gly
 500 505 510

Val Val Glu Gln Gly Ser Asn Ser Gln Leu Met Ala Val Gln Tyr Thr
 515 520 525

Glu Thr Thr Ser Ser Ile Ser Arg Asn Ser Gly Ser Glu Leu Gln Val
 530 535 540

Tyr Tyr Ala Ser Pro Arg Ser Tyr Gln Asp Phe Phe Glu Ala Ile Arg
 545 550 555 560

Protein Complexes associated with APP-processing
 Met Arg Leu Leu Ala Tyr Val Ser Gly Leu Gly Phe Gly Ile Met Ser
 115 120 125

Gly Val Phe Ser Phe Val Asn Thr Leu Ser Asp Ser Leu Gly Pro Gly
 130 135 140

Thr Val Gly Ile His Gly Asp Ser Pro Gln Phe Phe Leu Tyr Ser Ala
 145 150 155 160

Phe Met Thr Leu Val Ile Ile Leu Leu His Val Phe Trp Gly Ile Val
 165 170 175

Phe Phe Asp Gly Cys Glu Lys Lys Lys Trp Gly Ile Leu Leu Ile Val
 180 185 190

Leu Leu Thr His Leu Leu Val Ser Ala Gln Thr Phe Ile Ser Ser Tyr
 195 200 205

Tyr Gly Ile Asn Leu Ala Ser Ala Phe Ile Ile Leu Val Leu Met Gly
 210 215 220

Thr Trp Ala Phe Leu Ala Ala Gly Gly Ser Cys Arg Ser Leu Lys Leu
 225 230 235 240

Cys Leu Leu Cys Gln Asp Lys Asn Phe Leu Leu Tyr Asn Gln Arg Ser
 245 250 255

Arg

<210> 209

<211> 643

<212> PRT

<213> Homo sapiens

<400> 209

Met Pro Leu Leu Phe Leu Glu Arg Phe Pro Trp Pro Ser Leu Arg Thr
 1 5 10 15

Tyr Thr Gly Leu Ser Gly Leu Ala Leu Leu Gly Thr Ile Ile Ser Ala
 20 25 30

Tyr Arg Ala Leu Ser Gln Pro Glu Ala Gly Pro Gly Glu Pro Asp Gln
 35 40 45

Leu Thr Ala Ser Leu Gln Pro Glu Pro Pro Ala Pro Ala Arg Pro Ser
 50 55 60

Protein Complexes associated with APP-processing

Ala Gly Gly Pro Arg Ala Arg Asp Val Ala Gln Tyr Leu Leu Ser Asp
 65 70 75 80

Ser Leu Phe Val Trp Val Leu Val Asn Thr Ala Cys Cys Val Leu Met
 85 90 95

Leu Val Ala Lys Leu Ile Gln Cys Ile Val Phe Gly Pro Leu Arg Val
 100 105 110

Ser Glu Arg Gln His Leu Lys Asp Lys Phe Trp Asn Phe Ile Phe Tyr
 115 120 125

Lys Phe Ile Phe Ile Phe Gly Val Leu Asn Val Gln Thr Val Glu Glu
 130 135 140

Val Val Met Trp Cys Leu Trp Phe Ala Gly Leu Val Phe Leu His Leu
 145 150 155 160

Met Val Gln Leu Cys Lys Asp Arg Phe Glu Tyr Leu Ser Phe Ser Pro
 165 170 175

Thr Thr Pro Met Ser Ser His Gly Arg Val Leu Ser Leu Leu Val Ala
 180 185 190

Met Leu Leu Ser Cys Cys Gly Leu Ala Ala Val Cys Ser Ile Thr Gly
 195 200 205

Tyr Thr His Gly Met His Thr Leu Ala Phe Met Ala Ala Glu Ser Leu
 210 215 220

Leu Val Thr Val Arg Thr Ala His Val Ile Leu Arg Tyr Val Ile His
 225 230 235 240

Leu Trp Asp Leu Asn His Glu Gly Thr Trp Glu Gly Lys Gly Thr Tyr
 245 250 255

Val Tyr Tyr Thr Asp Phe Val Met Glu Leu Thr Leu Leu Ser Leu Asp
 260 265 270

Leu Met His His Ile His Met Leu Leu Phe Gly Asn Ile Trp Leu Ser
 275 280 285

Met Ala Ser Leu Val Ile Phe Met Gln Leu Arg Tyr Leu Phe His Glu
 290 295 300

Val Gln Arg Arg Ile Arg Arg His Lys Asn Tyr Leu Arg Val Val Gly
 305 310 315 320

Asn Met Glu Ala Arg Phe Ala Val Ala Thr Pro Glu Glu Leu Ala Val
 325 330 335

Protein Complexes associated with APP-processing

Asn Asn Asp Asp Cys Ala Ile Cys Trp Asp Ser Met Gln Ala Ala Arg
 340 345 350

Lys Leu Pro Cys Gly His Leu Phe His Asn Ser Cys Leu Arg Ser Trp
 355 360 365

Leu Glu Gln Asp Thr Ser Cys Pro Thr Cys Arg Met Ser Leu Asn Ile
 370 375 380

Ala Asp Asn Asn Arg Val Arg Glu Glu His Gln Gly Glu Asn Leu Asp
 385 390 395 400

Glu Asn Leu Val Pro Val Ala Ala Ala Glu Gly Arg Pro Arg Leu Asn
 405 410 415

Gln His Asn His Phe Phe His Phe Asp Gly Ser Arg Ile Ala Ser Trp
 420 425 430

Leu Pro Ser Phe Ser Val Glu Val Met His Thr Thr Asn Ile Leu Gly
 435 440 445

Ile Thr Gln Ala Ser Asn Ser Gln Leu Asn Ala Met Ala His Gln Ile
 450 455 460

Gln Glu Met Phe Pro Gln Val Pro Tyr His Leu Val Leu Gln Asp Leu
 465 470 475 480

Gln Leu Thr Arg Ser Val Glu Ile Thr Thr Asp Asn Ile Leu Glu Gly
 485 490 495

Arg Ile Gln Val Pro Phe Pro Thr Gln Arg Ser Asp Ser Ile Arg Pro
 500 505 510

Ala Leu Asn Ser Pro Val Glu Arg Pro Ser Ser Asp Gln Glu Glu Gly
 515 520 525

Glu Thr Ser Ala Gln Thr Glu Arg Val Pro Leu Asp Leu Ser Pro Arg
 530 535 540

Leu Glu Glu Thr Leu Asp Phe Gly Glu Val Glu Val Glu Pro Ser Glu
 545 550 555 560

Val Glu Asp Phe Glu Ala Arg Gly Ser Arg Phe Ser Lys Ser Ala Asp
 565 570 575

Glu Arg Gln Arg Met Leu Val Gln Arg Lys Asp Glu Leu Leu Gln Gln
 580 585 590

Ala Arg Lys Arg Phe Leu Asn Lys Ser Ser Glu Asp Asp Ala Ala Ser
 595 600 605

Protein Complexes associated with APP-processing

Glu Ser Phe Leu Pro Leu Glu Gly Ala Ser Ser Asp Pro Val Thr Leu
 610 615 620

Arg Arg Arg Met Leu Ala Ala Ala Ala Glu Arg Arg Leu Gln Lys Gln
 625 630 635 640

Gln Thr Ser

<210> 210

<211> 559

<212> PRT

<213> Homo sapiens

<400> 210

Met Ala Thr Ala Leu Ser Glu Glu Glu Leu Asp Asn Glu Asp Tyr Tyr
 1 5 10 15

Ser Leu Leu Asn Val Arg Arg Glu Ala Ser Ser Glu Glu Leu Lys Ala
 20 25 30

Ala Tyr Arg Arg Leu Cys Met Leu Tyr His Pro Asp Lys His Arg Asp
 35 40 45

Pro Glu Leu Lys Ser Gln Ala Glu Arg Leu Phe Asn Leu Val His Gln
 50 55 60

Ala Tyr Glu Val Leu Ser Asp Pro Gln Thr Arg Ala Ile Tyr Asp Ile
 65 70 75 80

Tyr Gly Lys Arg Gly Leu Glu Met Glu Gly Trp Glu Val Val Glu Arg
 85 90 95

Arg Arg Thr Pro Ala Glu Ile Arg Glu Glu Phe Glu Arg Leu Gln Arg
 100 105 110

Glu Arg Glu Glu Arg Arg Leu Gln Gln Arg Thr Asn Pro Lys Gly Thr
 115 120 125

Ile Ser Val Gly Val Asp Ala Thr Asp Leu Phe Asp Arg Tyr Asp Glu
 130 135 140

Glu Tyr Glu Asp Val Ser Gly Ser Ser Phe Pro Gln Ile Glu Ile Asn
 145 150 155 160

Lys Met His Ile Ser Gln Ser Ile Glu Ala Pro Leu Thr Ala Thr Asp
 165 170 175

Protein Complexes associated with APP-processing

Thr Ala Ile Leu Ser Gly Ser Leu Ser Thr Gln Asn Gly Asn Gly Gly
180 185 190

Gly Ser Ile Asn Phe Ala Leu Arg Arg Val Thr Ser Ala Lys Gly Trp
195 200 205

Gly Glu Leu Glu Phe Gly Ala Gly Asp Leu Gln Gly Pro Leu Phe Gly
210 215 220

Leu Lys Leu Phe Arg Asn Leu Thr Pro Arg Cys Phe Val Thr Thr Asn
225 230 235 240

Cys Ala Leu Gln Phe Ser Ser Arg Gly Ile Arg Pro Gly Leu Thr Thr
245 250 255

Val Leu Ala Arg Asn Leu Asp Lys Asn Thr Met Gly Tyr Leu Gln Trp
260 265 270

Arg Trp Gly Ile Gln Ser Ala Met Asn Thr Ser Ile Val Arg Asp Thr
275 280 285

Lys Thr Ser His Phe Thr Val Ala Leu Gln Leu Gly Ile Pro His Ser
290 295 300

Phe Ala Leu Ile Ile Tyr Gln His Lys Phe Gln Asp Asp Asp Gln Thr
305 310 315 320

Arg Val Lys Gly Ser Leu Lys Ala Gly Phe Phe Gly Thr Val Val Glu
325 330 335

Tyr Gly Ala Glu Arg Lys Ile Ser Arg His Ser Val Leu Gly Ala Ala
340 345 350

Val Ser Val Gly Val Pro Gln Gly Val Ser Leu Lys Val Lys Leu Asn
355 360 365

Arg Ala Ser Gln Thr Tyr Phe Phe Pro Ile His Leu Thr Asp Gln Leu
370 375 380

Leu Pro Ser Ala Met Phe Tyr Ala Thr Val Gly Pro Leu Val Val Tyr
385 390 395 400

Phe Ala Met His Arg Leu Ile Ile Lys Pro Tyr Leu Arg Ala Gln Lys
405 410 415

Glu Lys Glu Leu Glu Lys Gln Arg Glu Ser Ala Ala Thr Asp Val Leu
420 425 430

Gln Lys Lys Gln Glu Ala Glu Ser Ala Val Arg Leu Met Gln Glu Ser
435 440 445

Protein Complexes associated with APP-processing

Val Arg Arg Ile Ile Glu Ala Glu Glu Ser Arg Met Gly Leu Ile Ile
 450 455 460

Val Asn Ala Trp Tyr Gly Lys Phe Val Asn Asp Lys Ser Arg Lys Ser
 465 470 475 480

Glu Lys Val Lys Val Ile Asp Val Thr Val Pro Leu Gln Cys Leu Val
 485 490 495

Lys Asp Ser Lys Leu Ile Leu Thr Glu Ala Ser Lys Ala Gly Leu Pro
 500 505 510

Gly Phe Tyr Asp Pro Cys Val Gly Glu Glu Lys Asn Leu Lys Val Leu
 515 520 525

Tyr Gln Phe Arg Gly Val Leu His Gln Val Met Val Leu Asp Ser Glu
 530 535 540

Ala Leu Arg Ile Pro Lys Gln Ser His Arg Ile Asp Thr Asp Gly
 545 550 555

<210> 211

<211> 400

<212> PRT

<213> Homo sapiens

<400> 211

Met Ala Ala Asn Tyr Ser Ser Thr Ser Thr Arg Arg Glu His Val Lys
 1 5 10 15

Val Lys Thr Ser Ser Gln Pro Gly Phe Leu Glu Arg Leu Ser Glu Thr
 20 25 30

Ser Gly Gly Met Phe Val Gly Leu Met Ala Phe Leu Leu Ser Phe Tyr
 35 40 45

Leu Ile Phe Thr Asn Glu Gly Arg Ala Leu Lys Thr Ala Thr Ser Leu
 50 55 60

Ala Glu Gly Leu Ser Leu Val Val Ser Pro Asp Ser Ile His Ser Val
 65 70 75 80

Ala Pro Glu Asn Glu Gly Arg Leu Val His Ile Ile Gly Ala Leu Arg
 85 90 95

Thr Ser Lys Leu Leu Ser Asp Pro Asn Tyr Gly Val His Leu Pro Ala
 100 105 110

Protein Complexes associated with APP-processing

Val Lys Leu Arg Arg His Val Glu Met Tyr Gln Trp Val Glu Thr Glu
115 120 125

Glu Ser Arg Glu Tyr Thr Glu Asp Gly Gln Val Lys Lys Glu Thr Arg
130 135 140

Tyr Ser Tyr Asn Thr Glu Trp Arg Ser Glu Ile Ile Asn Ser Lys Asn
145 150 155 160

Phe Asp Arg Glu Ile Gly His Lys Asn Pro Ser Ala Met Ala Val Glu
165 170 175

Ser Phe Met Ala Thr Ala Pro Phe Val Gln Ile Gly Arg Phe Phe Leu
180 185 190

Ser Ser Gly Leu Ile Asp Lys Val Asp Asn Phe Lys Ser Leu Ser Leu
195 200 205

Ser Lys Leu Glu Asp Pro His Val Asp Ile Ile Arg Arg Gly Asp Phe
210 215 220

Phe Tyr His Ser Glu Asn Pro Lys Tyr Pro Glu Val Gly Asp Leu Arg
225 230 235 240

Val Ser Phe Ser Tyr Ala Gly Leu Ser Gly Asp Asp Pro Asp Leu Gly
245 250 255

Pro Ala His Val Val Thr Val Ile Ala Arg Gln Arg Gly Asp Gln Leu
260 265 270

Val Pro Phe Ser Thr Lys Ser Gly Asp Thr Leu Leu Leu Leu His His
275 280 285

Gly Asp Phe Ser Ala Glu Glu Val Phe His Arg Glu Leu Arg Ser Asn
290 295 300

Ser Met Lys Thr Trp Gly Leu Arg Ala Ala Gly Trp Met Ala Met Phe
305 310 315 320

Met Gly Leu Asn Leu Met Thr Arg Ile Leu Tyr Thr Leu Val Asp Trp
325 330 335

Phe Pro Val Phe Arg Asp Leu Val Asn Ile Gly Leu Lys Ala Phe Ala
340 345 350

Phe Cys Val Ala Thr Ser Leu Thr Leu Leu Thr Val Ala Ala Gly Trp
355 360 365

Leu Phe Tyr Arg Pro Leu Trp Ala Leu Leu Ile Ala Gly Leu Ala Leu
370 375 380

Protein Complexes associated with APP-processing

Val Pro Ile Leu Val Ala Arg Thr Arg Val Pro Ala Lys Lys Leu Glu
 385 390 395 400

<210> 212

<211> 1323

<212> PRT

<213> Homo sapiens

<400> 212

Met Glu Asp Gly Gly Leu Thr Ala Phe Glu Glu Asp Gln Arg Cys Leu
 1 5 10 15

Ser Gln Ser Leu Pro Leu Pro Val Ser Ala Glu Gly Pro Ala Ala Gln
 20 25 30

Thr Thr Ala Glu Pro Ser Arg Ser Phe Ser Ser Ala His Arg His Leu
 35 40 45

Ser Arg Arg Asn Gly Leu Ser Arg Leu Cys Gln Ser Arg Thr Ala Leu
 50 55 60

Ser Glu Asp Arg Trp Ser Ser Tyr Cys Leu Ser Ser Leu Ala Ala Gln
 65 70 75 80

Asn Ile Cys Thr Ser Lys Leu His Cys Pro Ala Ala Pro Glu His Thr
 85 90 95

Asp Pro Ser Glu Pro Arg Gly Ser Val Ser Cys Cys Ser Leu Leu Arg
 100 105 110

Gly Leu Ser Ser Gly Trp Ser Ser Pro Leu Leu Pro Ala Pro Val Cys
 115 120 125

Asn Pro Asn Lys Ala Ile Phe Thr Val Asp Ala Lys Thr Thr Glu Ile
 130 135 140

Leu Val Ala Asn Asp Lys Ala Cys Gly Leu Leu Gly Tyr Ser Ser Gln
 145 150 155 160

Asp Leu Ile Gly Gln Lys Leu Thr Gln Phe Phe Leu Arg Ser Asp Ser
 165 170 175

Asp Val Val Glu Ala Leu Ser Glu Glu His Met Glu Ala Asp Gly His
 180 185 190

Ala Ala Val Val Phe Gly Thr Val Val Asp Ile Ile Ser Arg Ser Gly
 195 200 205

Protein Complexes associated with APP-processing

Glu Lys Ile Pro Val Ser Val Trp Met Lys Arg Met Arg Gln Glu Arg
 210 215 220

Arg Leu Cys Cys Val Val Val Leu Glu Pro Val Glu Arg Val Ser Thr
 225 230 235 240

Trp Val Ala Phe Gln Ser Asp Gly Thr Val Thr Ser Cys Asp Ser Leu
 245 250 255

Phe Ala His Leu His Gly Tyr Val Ser Gly Glu Asp Val Ala Gly Gln
 260 265 270

His Ile Thr Asp Leu Ile Pro Ser Val Gln Leu Pro Pro Ser Gly Gln
 275 280 285

His Ile Pro Lys Asn Leu Lys Ile Gln Arg Ser Val Gly Arg Ala Arg
 290 295 300

Asp Gly Thr Thr Phe Pro Leu Ser Leu Lys Leu Lys Ser Gln Pro Ser
 305 310 315 320

Ser Glu Glu Ala Thr Thr Gly Glu Ala Ala Pro Val Ser Gly Tyr Arg
 325 330 335

Ala Ser Val Trp Val Phe Cys Thr Ile Ser Gly Leu Ile Thr Leu Leu
 340 345 350

Pro Asp Gly Thr Ile His Gly Ile Asn His Ser Phe Ala Leu Thr Leu
 355 360 365

Phe Gly Tyr Gly Lys Thr Glu Leu Leu Gly Lys Asn Ile Thr Phe Leu
 370 375 380

Ile Pro Gly Phe Tyr Ser Tyr Met Asp Leu Ala Tyr Asn Ser Ser Leu
 385 390 395 400

Gln Leu Pro Asp Leu Ala Ser Cys Leu Asp Val Gly Asn Glu Ser Gly
 405 410 415

Cys Gly Glu Arg Thr Leu Asp Pro Trp Gln Gly Gln Asp Pro Ala Glu
 420 425 430

Gly Gly Gln Asp Pro Arg Ile Asn Val Val Leu Ala Gly Gly His Val
 435 440 445

Val Pro Arg Asp Glu Ile Arg Lys Leu Met Glu Ser Gln Asp Ile Phe
 450 455 460

Thr Gly Thr Gln Thr Glu Leu Ile Ala Gly Gly Gln Leu Leu Ser Cys
 465 470 475 480

Protein Complexes associated with APP-processing
 Leu Ser Pro Gln Pro Ala Pro Gly Val Asp Asn Val Pro Glu Gly Ser
 485 490 495

Leu Pro Val His Gly Glu Gln Ala Leu Pro Lys Asp Gln Gln Ile Thr
 500 505 510

Ala Leu Gly Arg Glu Glu Pro Val Ala Ile Glu Ser Pro Gly Gln Asp
 515 520 525

Leu Leu Gly Glu Ser Arg Ser Glu Pro Val Asp Val Lys Pro Phe Ala
 530 535 540

Ser Cys Glu Asp Ser Glu Ala Pro Val Pro Ala Glu Asp Gly Gly Ser
 545 550 555 560

Asp Ala Gly Met Cys Gly Leu Cys Gln Lys Ala Gln Leu Glu Arg Met
 565 570 575

Gly Val Ser Gly Pro Ser Gly Ser Asp Leu Trp Ala Gly Ala Ala Val
 580 585 590

Ala Lys Pro Gln Ala Lys Gly Gln Leu Ala Gly Gly Ser Leu Leu Met
 595 600 605

His Cys Pro Cys Tyr Gly Ser Glu Trp Gly Leu Trp Trp Arg Ser Gln
 610 615 620

Asp Leu Ala Pro Ser Pro Ser Gly Met Ala Gly Leu Ser Phe Gly Thr
 625 630 635 640

Pro Thr Leu Asp Glu Pro Trp Leu Gly Val Glu Asn Asp Arg Glu Glu
 645 650 655

Leu Gln Thr Cys Leu Ile Lys Glu Gln Leu Ser Gln Leu Ser Leu Ala
 660 665 670

Gly Ala Leu Asp Val Pro His Ala Glu Leu Val Pro Thr Glu Cys Gln
 675 680 685

Ala Val Thr Ala Pro Val Ser Ser Cys Asp Leu Gly Gly Arg Asp Leu
 690 695 700

Cys Gly Gly Cys Thr Gly Ser Ser Ser Ala Cys Tyr Ala Leu Ala Thr
 705 710 715 720

Asp Leu Pro Gly Gly Leu Glu Ala Val Glu Ala Gln Glu Val Asp Val
 725 730 735

Asn Ser Phe Ser Trp Asn Leu Lys Glu Leu Phe Phe Ser Asp Gln Thr
 740 745 750

Protein Complexes associated with APP-processing

Asp Gln Thr Ser Ser Asn Cys Ser Cys Ala Thr Ser Glu Leu Arg Glu
 755 760 765

Thr Pro Ser Ser Leu Ala Val Gly Ser Asp Pro Asp Val Gly Ser Leu
 770 775 780

Gln Glu Gln Gly Ser Cys Val Leu Asp Asp Arg Glu Leu Leu Leu Leu
 785 790 795 800

Thr Gly Thr Cys Val Asp Leu Gly Gln Gly Arg Arg Phe Arg Glu Ser
 805 810 815

Cys Val Gly His Asp Pro Thr Glu Pro Leu Glu Val Cys Leu Val Ser
 820 825 830

Ser Glu His Tyr Ala Ala Ser Asp Arg Glu Ser Pro Gly His Val Pro
 835 840 845

Ser Thr Leu Asp Ala Gly Pro Glu Asp Thr Cys Pro Ser Ala Glu Glu
 850 855 860

Pro Arg Leu Asn Val Gln Val Thr Ser Thr Pro Val Ile Val Met Arg
 865 870 875 880

Gly Ala Ala Gly Leu Gln Arg Glu Ile Gln Glu Gly Ala Tyr Ser Gly
 885 890 895

Ser Cys His His Arg Asp Gly Leu Arg Leu Ser Ile Gln Phe Glu Val
 900 905 910

Arg Arg Val Glu Leu Gln Gly Pro Thr Pro Leu Phe Cys Cys Trp Leu
 915 920 925

Val Lys Asp Leu Leu His Ser Gln Arg Asp Ser Ala Ala Arg Thr Arg
 930 935 940

Leu Phe Leu Ala Ser Leu Pro Gly Ser Thr His Ser Thr Ala Ala Glu
 945 950 955 960

Leu Thr Gly Pro Ser Leu Val Glu Val Leu Arg Ala Arg Pro Trp Phe
 965 970 975

Glu Glu Pro Pro Lys Ala Val Glu Leu Glu Gly Leu Ala Ala Cys Glu
 980 985 990

Gly Glu Tyr Ser Gln Lys Tyr Ser Thr Met Ser Pro Leu Gly Ser Gly
 995 1000 1005

Ala Phe Gly Phe Val Trp Thr Ala Val Asp Lys Glu Lys Asn Lys
 1010 1015 1020

Protein Complexes associated with APP-processing

Glu Val Val Lys Phe Ile Lys Lys Glu Lys Val Leu Glu Asp
 1025 1030 1035

Cys Trp Ile Glu Asp Pro Lys Leu Gly Lys Val Thr Leu Glu Ile
 1040 1045 1050

Ala Ile Leu Ser Arg Val Glu His Ala Asn Ile Ile Lys Val Leu
 1055 1060 1065

Asp Ile Phe Glu Asn Gln Gly Phe Phe Gln Leu Val Met Glu Lys
 1070 1075 1080

His Gly Ser Gly Leu Asp Leu Phe Ala Phe Ile Asp Arg His Pro
 1085 1090 1095

Arg Leu Asp Glu Pro Leu Ala Ser Tyr Ile Phe Arg Gln Leu Val
 1100 1105 1110

Ser Ala Val Gly Tyr Leu Arg Leu Lys Asp Ile Ile His Arg Asp
 1115 1120 1125

Ile Lys Asp Glu Asn Ile Val Ile Ala Glu Asp Phe Thr Ile Lys
 1130 1135 1140

Leu Ile Asp Phe Gly Ser Ala Ala Tyr Leu Glu Arg Gly Lys Leu
 1145 1150 1155

Phe Tyr Thr Phe Cys Gly Thr Ile Glu Tyr Cys Ala Pro Glu Val
 1160 1165 1170

Leu Met Gly Asn Pro Tyr Arg Gly Pro Glu Leu Glu Met Trp Ser
 1175 1180 1185

Leu Gly Val Thr Leu Tyr Thr Leu Val Phe Glu Glu Asn Pro Phe
 1190 1195 1200

Cys Glu Leu Glu Glu Thr Val Glu Ala Ala Ile His Pro Pro Tyr
 1205 1210 1215

Leu Val Ser Lys Glu Leu Met Ser Leu Val Ser Gly Leu Leu Gln
 1220 1225 1230

Pro Val Pro Glu Arg Arg Thr Thr Leu Glu Lys Leu Val Thr Asp
 1235 1240 1245

Pro Trp Val Thr Gln Pro Val Asn Leu Ala Asp Tyr Thr Trp Glu
 1250 1255 1260

Glu Val Cys Arg Val Asn Lys Pro Glu Ser Gly Val Leu Ser Ala
 1265 1270 1275

Protein Complexes associated with APP-processing
 Ala Ser Leu Glu Met Gly Asn Arg Ser Leu Ser Asp Val Ala Gln
 1280 1285 1290

Ala Gln Glu Leu Cys Gly Gly Pro Val Pro Gly Glu Ala Pro Asn
 1295 1300 1305

Gly Gln Gly Cys Leu His Pro Gly Asp Pro Arg Leu Leu Thr Ser
 1310 1315 1320

<210> 213

<211> 968

<212> PRT

<213> Homo sapiens

<400> 213

Met Val Asn Ser Ser Arg Val Gln Pro Gln Gln Pro Gly Asp Ala Lys
 1 5 10 15

Arg Pro Pro Ala Pro Arg Ala Pro Asp Pro Gly Arg Leu Met Ala Gly
 20 25 30

Cys Ala Ala Val Gly Ala Ser Leu Ala Ala Pro Gly Arg Leu Cys Glu
 35 40 45

Gln Arg Gly Leu Glu Ile Glu Met Gln Arg Ile Arg Gln Ala Ala Ala
 50 55 60

Arg Asp Pro Pro Ala Gly Ala Ala Ala Ser Pro Ser Pro Pro Leu Ser
 65 70 75 80

Ser Cys Ser Arg Gln Ala Trp Ser Arg Asp Asn Pro Gly Phe Glu Ala
 85 90 95

Glu Glu Glu Glu Glu Glu Val Glu Gly Glu Glu Gly Gly Met Val Val
 100 105 110

Glu Met Asp Val Glu Trp Arg Pro Gly Ser Arg Arg Ser Ala Ala Ser
 115 120 125

Ser Ala Val Ser Ser Val Gly Ala Arg Ser Arg Gly Leu Gly Gly Tyr
 130 135 140

His Gly Ala Gly His Pro Ser Gly Arg Arg Arg Arg Arg Glu Asp Gln
 145 150 155 160

Gly Pro Pro Cys Pro Ser Pro Val Gly Gly Gly Asp Pro Leu His Arg
 165 170 175

Protein Complexes associated with APP-processing

His Leu Pro Leu Glu Gly Gln Pro Pro Arg Val Ala Trp Ala Glu Arg
 180 185 190

Leu Val Arg Gly Leu Arg Gly Leu Trp Gly Thr Arg Leu Met Glu Glu
 195 200 205

Ser Ser Thr Asn Arg Glu Lys Tyr Leu Lys Ser Val Leu Arg Glu Leu
 210 215 220

Val Thr Tyr Leu Leu Phe Leu Ile Val Leu Cys Ile Leu Thr Tyr Gly
 225 230 235 240

Met Met Ser Ser Asn Val Tyr Tyr Tyr Thr Arg Met Met Ser Gln Leu
 245 250 255

Phe Leu Asp Thr Pro Val Ser Lys Thr Glu Lys Thr Asn Phe Lys Thr
 260 265 270

Leu Ser Ser Met Glu Asp Phe Trp Lys Phe Thr Glu Gly Ser Leu Leu
 275 280 285

Asp Gly Leu Tyr Trp Lys Met Gln Pro Ser Asn Gln Thr Glu Ala Asp
 290 295 300

Asn Arg Ser Phe Ile Phe Tyr Glu Asn Leu Leu Leu Gly Val Pro Arg
 305 310 315 320

Ile Arg Gln Leu Arg Val Arg Asn Gly Ser Cys Ser Ile Pro Gln Asp
 325 330 335

Leu Arg Asp Glu Ile Lys Glu Cys Tyr Asp Val Tyr Ser Val Ser Ser
 340 345 350

Glu Asp Arg Ala Pro Phe Gly Pro Arg Asn Gly Thr Ala Trp Ile Tyr
 355 360 365

Thr Ser Glu Lys Asp Leu Asn Gly Ser Ser His Trp Gly Ile Ile Ala
 370 375 380

Thr Tyr Ser Gly Ala Gly Tyr Tyr Leu Asp Leu Ser Arg Thr Arg Glu
 385 390 395 400

Glu Thr Ala Ala Gln Val Ala Ser Leu Lys Lys Asn Val Trp Leu Asp
 405 410 415

Arg Gly Thr Arg Ala Thr Phe Ile Asp Phe Ser Val Tyr Asn Ala Asn
 420 425 430

Ile Asn Leu Phe Cys Val Val Arg Leu Leu Val Glu Phe Pro Ala Thr
 435 440 445

Protein Complexes associated with APP-processing

Gly Gly Val Ile Pro Ser Trp Gln Phe Gln Pro Leu Lys Leu Ile Arg
 450 455 460

Tyr Val Thr Thr Phe Asp Phe Phe Leu Ala Ala Cys Glu Ile Ile Phe
 465 470 475 480

Cys Phe Phe Ile Phe Tyr Tyr Val Val Glu Glu Ile Leu Glu Ile Arg
 485 490 495

Ile His Lys Leu His Tyr Phe Arg Ser Phe Trp Asn Cys Leu Asp Val
 500 505 510

Val Ile Val Val Leu Ser Val Val Ala Ile Gly Ile Asn Ile Tyr Arg
 515 520 525

Thr Ser Asn Val Glu Val Leu Leu Gln Phe Leu Glu Asp Gln Asn Thr
 530 535 540

Phe Pro Asn Phe Glu His Leu Ala Tyr Trp Gln Ile Gln Phe Asn Asn
 545 550 555 560

Ile Ala Ala Val Thr Val Phe Phe Val Trp Ile Lys Leu Phe Lys Phe
 565 570 575

Ile Asn Phe Asn Arg Thr Met Ser Gln Leu Ser Thr Thr Met Ser Arg
 580 585 590

Cys Ala Lys Asp Leu Phe Gly Phe Ala Ile Met Phe Phe Ile Ile Phe
 595 600 605

Leu Ala Tyr Ala Gln Leu Ala Tyr Leu Val Phe Gly Thr Gln Val Asp
 610 615 620

Asp Phe Ser Thr Phe Gln Glu Cys Ile Phe Thr Gln Phe Arg Ile Ile
 625 630 635 640

Leu Gly Asp Ile Asn Phe Ala Glu Ile Glu Glu Ala Asn Arg Val Leu
 645 650 655

Gly Pro Ile Tyr Phe Thr Thr Phe Val Phe Phe Met Phe Phe Ile Leu
 660 665 670

Leu Asn Met Phe Leu Ala Ile Ile Asn Asp Thr Tyr Ser Glu Val Lys
 675 680 685

Ser Asp Leu Ala Gln Gln Lys Ala Glu Met Glu Leu Ser Asp Leu Ile
 690 695 700

Arg Lys Gly Tyr His Lys Ala Leu Val Lys Leu Lys Leu Lys Lys Asn
 705 710 715 720

Protein Complexes associated with APP-processing

Thr Val Asp Asp Ile Ser Glu Ser Leu Arg Gln Gly Gly Gly Lys Leu
 725 730 735

Asn Phe Asp Glu Leu Arg Gln Asp Leu Lys Gly Lys Gly His Thr Asp
 740 745 750

Ala Glu Ile Glu Ala Ile Phe Thr Lys Tyr Asp Gln Asp Gly Asp Gln
 755 760 765

Glu Leu Thr Glu His Glu His Gln Gln Met Arg Asp Asp Leu Glu Lys
 770 775 780

Glu Arg Glu Asp Leu Asp Leu Asp His Ser Ser Leu Pro Arg Pro Met
 785 790 795 800

Ser Ser Arg Ser Phe Pro Arg Ser Leu Asp Asp Ser Glu Glu Asp Asp
 805 810 815

Asp Glu Asp Ser Gly His Ser Ser Arg Arg Arg Gly Ser Ile Ser Ser
 820 825 830

Gly Val Ser Tyr Glu Glu Phe Gln Val Leu Val Arg Arg Val Asp Arg
 835 840 845

Met Glu His Ser Ile Gly Ser Ile Val Ser Lys Ile Asp Ala Val Ile
 850 855 860

Val Lys Leu Glu Ile Met Glu Arg Ala Lys Leu Lys Arg Arg Glu Val
 865 870 875 880

Leu Gly Arg Leu Leu Asp Gly Val Ala Glu Asp Glu Arg Leu Gly Arg
 885 890 895

Asp Ser Glu Ile His Arg Glu Gln Met Glu Arg Leu Val Arg Glu Glu
 900 905 910

Leu Glu Arg Trp Glu Ser Asp Asp Ala Ala Ser Gln Ile Ser His Gly
 915 920 925

Leu Gly Thr Pro Val Gly Leu Asn Gly Gln Pro Arg Pro Arg Ser Ser
 930 935 940

Arg Pro Ser Ser Ser Gln Ser Thr Glu Gly Met Glu Gly Ala Gly Gly
 945 950 955 960

Asn Gly Ser Ser Asn Val His Val
 965

<210> 214

<211> 776

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 214

Met Glu Ile Gly Trp Met His Asn Arg Arg Gln Arg Gln Val Leu Val
 1 5 10 15

Phe Phe Val Leu Leu Ser Leu Ser Gly Ala Gly Ala Glu Leu Gly Ser
 20 25 30

Tyr Ser Val Val Glu Glu Thr Glu Arg Gly Ser Phe Val Ala Asn Leu
 35 40 45

Gly Lys Asp Leu Gly Leu Gly Leu Thr Glu Met Ser Thr Arg Lys Ala
 50 55 60

Arg Ile Ile Ser Gln Gly Asn Lys Gln His Leu Gln Leu Lys Ala Gln
 65 70 75 80

Thr Gly Asp Leu Leu Ile Asn Glu Lys Leu Asp Arg Glu Glu Leu Cys
 85 90 95

Gly Pro Thr Glu Pro Cys Ile Leu His Phe Gln Val Leu Met Glu Asn
 100 105 110

Pro Leu Glu Ile Phe Gln Ala Glu Leu Arg Val Ile Asp Ile Asn Asp
 115 120 125

His Ser Pro Met Phe Thr Glu Lys Glu Met Ile Leu Lys Ile Pro Glu
 130 135 140

Asn Ser Pro Leu Gly Thr Glu Phe Pro Leu Asn His Ala Leu Asp Leu
 145 150 155 160

Asp Val Gly Ser Asn Asn Val Gln Asn Tyr Lys Ile Ser Pro Ser Ser
 165 170 175

His Phe Arg Val Leu Ile His Glu Phe Arg Asp Gly Arg Lys Tyr Pro
 180 185 190

Glu Leu Val Leu Asp Lys Glu Leu Asp Arg Glu Glu Glu Pro Gln Leu
 195 200 205

Arg Leu Thr Leu Thr Ala Leu Asp Gly Gly Ser Pro Pro Arg Ser Gly
 210 215 220

Thr Ala Gln Val Arg Ile Glu Val Val Asp Ile Asn Asp Asn Ala Pro
 225 230 235 240

Protein Complexes associated with APP-processing
 Glu Phe Glu Gln Pro Ile Tyr Lys Val Gln Ile Pro Glu Asn Ser Pro
 245 250 255

Leu Gly Ser Leu Val Ala Thr Val Ser Ala Arg Asp Leu Asp Gly Gly
 260 265 270

Ala Asn Gly Lys Ile Ser Tyr Thr Leu Phe Gln Pro Ser Glu Asp Ile
 275 280 285

Ser Lys Thr Leu Glu Val Asn Pro Met Thr Gly Glu Val Arg Leu Arg
 290 295 300

Lys Gln Val Asp Phe Glu Met Val Thr Ser Tyr Glu Val Arg Ile Lys
 305 310 315 320

Ala Thr Asp Gly Gly Gly Leu Ser Gly Lys Cys Thr Leu Leu Leu Gln
 325 330 335

Val Val Asp Val Asn Asp Asn Pro Pro Gln Val Thr Met Ser Ala Leu
 340 345 350

Thr Ser Pro Ile Pro Glu Asn Ser Pro Glu Ile Val Val Ala Val Phe
 355 360 365

Ser Val Ser Asp Pro Asp Ser Gly Asn Asn Gly Lys Thr Ile Ser Ser
 370 375 380

Ile Gln Glu Asp Leu Pro Phe Leu Leu Lys Pro Ser Val Lys Asn Phe
 385 390 395 400

Tyr Thr Leu Val Thr Glu Arg Ala Leu Asp Arg Glu Ala Arg Ala Glu
 405 410 415

Tyr Asn Ile Thr Leu Thr Val Thr Asp Met Gly Thr Pro Arg Leu Lys
 420 425 430

Thr Glu His Asn Ile Thr Val Gln Ile Ser Asp Val Asn Asp Asn Ala
 435 440 445

Pro Thr Phe Thr Gln Thr Ser Tyr Thr Leu Phe Val Arg Glu Asn Asn
 450 455 460

Ser Pro Ala Leu His Ile Gly Ser Val Ser Ala Thr Asp Arg Asp Ser
 465 470 475 480

Gly Thr Asn Ala Gln Val Thr Tyr Ser Leu Leu Pro Pro Gln Asp Pro
 485 490 495

His Leu Pro Leu Ala Ser Leu Val Ser Ile Asn Ala Asp Asn Gly His
 500 505 510

Protein Complexes associated with APP-processing

Pro Ile Ile Pro Asn Phe Ser Pro
770 775

Protein Complexes associated with APP-processing

<210> 215

<211> 934

<212> PRT

<213> Homo sapiens

<400> 215

Met Val Pro Glu Ala Trp Arg Ser Gly Leu Val Ser Thr Gly Arg Val
 1 5 10 15

Val Gly Val Leu Leu Leu Leu Gly Ala Leu Asn Lys Ala Ser Thr Val
 20 25 30

Ile His Tyr Glu Ile Pro Glu Glu Arg Glu Lys Gly Phe Ala Val Gly
 35 40 45

Asn Val Val Ala Asn Leu Gly Leu Asp Leu Gly Ser Leu Ser Ala Arg
 50 55 60

Arg Phe Arg Val Val Ser Gly Ala Ser Arg Arg Phe Phe Glu Val Asn
 65 70 75 80

Arg Glu Thr Gly Glu Met Phe Val Asn Asp Arg Leu Asp Arg Glu Glu
 85 90 95

Leu Cys Gly Thr Leu Pro Ser Cys Thr Val Thr Leu Glu Leu Val Val
 100 105 110

Glu Asn Pro Leu Glu Leu Phe Ser Val Glu Val Val Ile Gln Asp Ile
 115 120 125

Asn Asp Asn Asn Pro Ala Phe Pro Thr Gln Glu Met Lys Leu Glu Ile
 130 135 140

Ser Glu Ala Val Ala Pro Gly Thr Arg Phe Pro Leu Glu Ser Ala His
 145 150 155 160

Asp Pro Asp Val Gly Ser Asn Ser Leu Gln Thr Tyr Glu Leu Ser Arg
 165 170 175

Asn Glu Tyr Phe Ala Leu Arg Val Gln Thr Arg Glu Asp Ser Thr Lys
 180 185 190

Tyr Ala Glu Leu Val Leu Glu Arg Ala Leu Asp Arg Glu Arg Glu Pro
 195 200 205

Ser Leu Gln Leu Val Leu Thr Ala Leu Asp Gly Gly Thr Pro Ala Leu
 210 215 220

Protein Complexes associated with APP-processing

Ser Ala Ser Leu Pro Ile His Ile Lys Val Leu Asp Ala Asn Asp Asn
 225 230 235 240

Ala Pro Val Phe Asn Gln Ser Leu Tyr Arg Ala Arg Val Leu Glu Asp
 245 250 255

Ala Pro Ser Gly Thr Arg Val Val Gln Val Leu Ala Thr Asp Leu Asp
 260 265 270

Glu Gly Pro Asn Gly Glu Ile Ile Tyr Ser Phe Gly Ser His Asn Arg
 275 280 285

Ala Gly Val Arg Gln Leu Phe Ala Leu Asp Leu Val Thr Gly Met Leu
 290 295 300

Thr Ile Lys Gly Arg Leu Asp Phe Glu Asp Thr Lys Leu His Glu Ile
 305 310 315 320

Tyr Ile Gln Ala Lys Asp Lys Gly Ala Asn Pro Glu Gly Ala His Cys
 325 330 335

Lys Val Leu Val Glu Val Val Asp Val Asn Asp Asn Ala Pro Glu Ile
 340 345 350

Thr Val Thr Ser Val Tyr Ser Pro Val Pro Glu Asp Ala Pro Leu Gly
 355 360 365

Thr Val Ile Ala Leu Leu Ser Val Thr Asp Leu Asp Ala Gly Glu Asn
 370 375 380

Gly Leu Val Thr Cys Glu Val Pro Pro Gly Leu Pro Phe Ser Leu Thr
 385 390 395 400

Ser Ser Leu Lys Asn Tyr Phe Thr Leu Lys Thr Ser Ala Asp Leu Asp
 405 410 415

Arg Glu Thr Val Pro Glu Tyr Asn Leu Ser Ile Thr Ala Arg Asp Ala
 420 425 430

Gly Thr Pro Ser Leu Ser Ala Leu Thr Ile Val Arg Val Gln Val Ser
 435 440 445

Asp Ile Asn Asp Asn Pro Pro Gln Ser Ser Gln Ser Ser Tyr Asp Val
 450 455 460

Tyr Ile Glu Glu Asn Asn Leu Pro Gly Ala Pro Ile Leu Asn Leu Ser
 465 470 475 480

Val Trp Asp Pro Asp Ala Pro Gln Asn Ala Arg Leu Ser Phe Phe Leu
 485 490 495

Protein Complexes associated with APP-processing

Leu Glu Gln Gly Ala Glu Thr Gly Leu Val Gly Arg Tyr Phe Thr Ile
500 505 510

Asn Arg Asp Asn Gly Ile Val Ser Ser Leu Val Pro Leu Asp Tyr Glu
515 520 525

Asp Arg Arg Glu Phe Glu Leu Thr Ala His Ile Ser Asp Gly Gly Thr
530 535 540

Pro Val Leu Ala Thr Asn Ile Ser Val Asn Ile Phe Val Thr Asp Arg
545 550 555 560

Asn Asp Asn Ala Pro Gln Val Leu Tyr Pro Arg Pro Gly Gly Ser Ser
565 570 575

Val Glu Met Leu Pro Arg Gly Thr Ser Ala Gly His Leu Val Ser Arg
580 585 590

Val Val Gly Trp Asp Ala Asp Ala Gly His Asn Ala Trp Leu Ser Tyr
595 600 605

Ser Leu Leu Gly Ser Pro Asn Gln Ser Leu Phe Ala Ile Gly Leu His
610 615 620

Thr Gly Gln Ile Ser Thr Ala Arg Pro Val Gln Asp Thr Asp Ser Pro
625 630 635 640

Arg Gln Thr Leu Thr Val Leu Ile Lys Asp Asn Gly Glu Pro Ser Leu
645 650 655

Ser Thr Thr Ala Thr Leu Thr Val Ser Val Thr Glu Asp Ser Pro Glu
660 665 670

Ala Arg Ala Glu Phe Pro Ser Gly Ser Ala Pro Arg Glu Gln Lys Lys
675 680 685

Asn Leu Thr Phe Tyr Leu Leu Leu Ser Leu Ile Leu Val Ser Val Gly
690 695 700

Phe Val Val Thr Val Phe Gly Val Ile Ile Phe Lys Val Tyr Lys Trp
705 710 715 720

Lys Gln Ser Arg Asp Leu Tyr Arg Ala Pro Val Ser Ser Leu Tyr Arg
725 730 735

Thr Pro Gly Pro Ser Leu His Ala Asp Ala Val Arg Gly Gly Leu Met
740 745 750

Ser Pro His Leu Tyr His Gln Val Tyr Leu Thr Thr Asp Ser Arg Arg
755 760 765

Protein Complexes associated with APP-processing
 Ser Asp Pro Leu Leu Lys Lys Pro Gly Ala Ala Ser Pro Leu Ala Ser
 770 775 780

Arg Gln Asn Thr Leu Arg Ser Cys Asp Pro Val Phe Tyr Arg Gln Val
 785 790 795 800

Leu Gly Ala Glu Ser Ala Pro Pro Gly Gln Gln Ala Pro Pro Asn Thr
 805 810 815

Asp Trp Arg Phe Ser Gln Ala Gln Arg Pro Gly Thr Ser Gly Ser Gln
 820 825 830

Asn Gly Asp Asp Thr Gly Thr Trp Pro Asn Asn Gln Phe Asp Thr Glu
 835 840 845

Met Leu Gln Ala Met Ile Leu Ala Ser Ala Ser Glu Ala Ala Asp Gly
 850 855 860

Ser Ser Thr Leu Gly Gly Gly Ala Gly Thr Met Gly Leu Ser Ala Arg
 865 870 875 880

Tyr Gly Pro Gln Phe Thr Leu Gln His Val Pro Asp Tyr Arg Gln Asn
 885 890 895

Val Tyr Ile Pro Gly Ser Asn Ala Thr Leu Thr Asn Ala Ala Gly Lys
 900 905 910

Arg Asp Gly Lys Ala Pro Ala Gly Gly Asn Gly Asn Lys Lys Lys Ser
 915 920 925

Gly Lys Lys Glu Lys Lys
 930

<210> 216

<211> 283

<212> PRT

<213> Homo sapiens

<400> 216

Met Cys Asn Thr Pro Thr Tyr Cys Asp Leu Gly Lys Ala Ala Lys Asp
 1 5 10 15

Val Phe Asn Lys Gly Tyr Gly Phe Gly Met Val Lys Ile Asp Leu Lys
 20 25 30

Thr Lys Ser Cys Ser Gly Val Glu Phe Ser Thr Ser Gly His Ala Tyr
 35 40 45

Protein Complexes associated with APP-processing
 Thr Asp Thr Gly Lys Ala Ser Gly Asn Leu Glu Thr Lys Tyr Lys Val
 50 55 60

Cys Asn Tyr Gly Leu Thr Phe Thr Gln Lys Trp Asn Thr Asp Asn Thr
 65 70 75 80

Leu Gly Thr Glu Ile Ser Trp Glu Asn Lys Leu Ala Glu Gly Leu Lys
 85 90 95

Leu Thr Leu Asp Thr Ile Phe Val Pro Asn Thr Gly Lys Lys Ser Gly
 100 105 110

Lys Leu Lys Ala Ser Tyr Lys Arg Asp Cys Phe Ser Val Gly Ser Asn
 115 120 125

Val Asp Ile Asp Phe Ser Gly Pro Thr Ile Tyr Gly Trp Ala Val Leu
 130 135 140

Ala Phe Glu Gly Trp Leu Ala Gly Tyr Gln Met Ser Phe Asp Thr Ala
 145 150 155 160

Lys Ser Lys Leu Ser Gln Asn Asn Phe Ala Leu Gly Tyr Lys Ala Ala
 165 170 175

Asp Phe Gln Leu His Thr His Val Asn Asp Gly Thr Glu Phe Gly Gly
 180 185 190

Ser Ile Tyr Gln Lys Val Asn Glu Lys Ile Glu Thr Ser Ile Asn Leu
 195 200 205

Ala Trp Thr Ala Gly Ser Asn Asn Thr Arg Phe Gly Ile Ala Ala Lys
 210 215 220

Tyr Met Leu Asp Cys Arg Thr Ser Leu Ser Ala Lys Val Asn Asn Ala
 225 230 235 240

Ser Leu Ile Gly Leu Gly Tyr Thr Gln Thr Leu Arg Pro Gly Val Lys
 245 250 255

Leu Thr Leu Ser Ala Leu Ile Asp Gly Lys Asn Phe Ser Ala Gly Gly
 260 265 270

His Lys Val Gly Leu Gly Phe Glu Leu Glu Ala
 275 280

<210> 217

<211> 703

<212> PRT

<213> Homo sapiens

Protein Complexes associated with APP-processing

<400> 217

Met Ala Glu Leu Met Leu Leu Ser Glu Ile Ala Asp Pro Thr Arg Phe
 1 5 10 15

Phe Thr Asp Asn Leu Leu Ser Pro Glu Asp Trp Gly Leu Gln Asn Ser
 20 25 30

Thr Leu Tyr Ser Gly Leu Asp Glu Val Ala Glu Glu Gln Thr Gln Leu
 35 40 45

Phe Arg Cys Pro Glu Gln Asp Val Pro Phe Asp Gly Ser Ser Leu Asp
 50 55 60

Val Gly Met Asp Val Ser Pro Ser Glu Pro Pro Trp Glu Leu Leu Pro
 65 70 75 80

Ile Phe Pro Asp Leu Gln Val Lys Ser Glu Pro Ser Ser Pro Cys Ser
 85 90 95

Ser Ser Ser Leu Ser Ser Glu Ser Ser Arg Leu Ser Thr Glu Pro Ser
 100 105 110

Ser Glu Ala Leu Gly Val Gly Glu Val Leu His Val Lys Thr Glu Ser
 115 120 125

Leu Ala Pro Pro Leu Cys Leu Leu Gly Asp Asp Pro Thr Ser Ser Phe
 130 135 140

Glu Thr Val Gln Ile Asn Val Ile Pro Thr Ser Asp Asp Ser Ser Asp
 145 150 155 160

Val Gln Thr Lys Ile Glu Pro Val Ser Pro Cys Ser Ser Val Asn Ser
 165 170 175

Glu Ala Ser Leu Leu Ser Ala Asp Ser Ser Ser Gln Ala Phe Ile Gly
 180 185 190

Glu Glu Val Leu Glu Val Lys Thr Glu Ser Leu Ser Pro Ser Gly Cys
 195 200 205

Leu Leu Trp Asp Val Pro Ala Pro Ser Leu Gly Ala Val Gln Ile Ser
 210 215 220

Met Gly Pro Ser Leu Asp Gly Ser Ser Gly Lys Ala Leu Pro Thr Arg
 225 230 235 240

Lys Pro Pro Leu Gln Pro Lys Pro Val Val Leu Thr Thr Val Pro Met
 245 250 255

Protein Complexes associated with APP-processing

Pro Ser Arg Ala Val Pro Pro Ser Thr Thr Val Leu Leu Gln Ser Leu
 260 265 270

Val Gln Pro Pro Pro Val Ser Pro Val Val Leu Ile Gln Gly Ala Ile
 275 280 285

Arg Val Gln Pro Glu Gly Pro Ala Pro Ser Leu Pro Arg Pro Glu Arg
 290 295 300

Lys Ser Ile Val Pro Ala Pro Met Pro Gly Asn Ser Cys Pro Pro Glu
 305 310 315 320

Val Asp Ala Lys Leu Leu Lys Arg Gln Gln Arg Met Ile Lys Asn Arg
 325 330 335

Glu Ser Ala Cys Gln Ser Arg Arg Lys Lys Lys Glu Tyr Leu Gln Gly
 340 345 350

Leu Glu Ala Arg Leu Gln Ala Val Leu Ala Asp Asn Gln Gln Leu Arg
 355 360 365

Arg Glu Asn Ala Ala Leu Arg Arg Arg Leu Glu Ala Leu Leu Ala Glu
 370 375 380

Asn Ser Glu Leu Lys Leu Gly Ser Gly Asn Arg Lys Val Val Cys Ile
 385 390 395 400

Met Val Phe Leu Leu Phe Ile Ala Phe Asn Phe Gly Pro Val Ser Ile
 405 410 415

Ser Glu Pro Pro Ser Ala Pro Ile Ser Pro Arg Met Asn Lys Gly Glu
 420 425 430

Pro Gln Pro Arg Arg His Leu Leu Gly Phe Ser Glu Gln Glu Pro Val
 435 440 445

Gln Gly Val Glu Pro Leu Gln Gly Ser Ser Gln Gly Pro Lys Glu Pro
 450 455 460

Gln Pro Ser Pro Thr Asp Gln Pro Ser Phe Ser Asn Leu Thr Ala Phe
 465 470 475 480

Pro Gly Gly Ala Lys Glu Leu Leu Leu Arg Asp Leu Asp Gln Leu Phe
 485 490 495

Leu Ser Ser Asp Cys Arg His Phe Asn Arg Thr Glu Ser Leu Arg Leu
 500 505 510

Ala Asp Glu Leu Ser Gly Trp Val Gln Arg His Gln Arg Gly Arg Arg
 515 520 525

Protein Complexes associated with APP-processing

Lys Ile Pro Gln Arg Ala Gln Glu Arg Gln Lys Ser Gln Pro Arg Lys
 530 535 540

Lys Ser Pro Pro Val Lys Ala Val Pro Ile Gln Pro Pro Gly Pro Pro
 545 550 555 560

Glu Arg Asp Ser Val Gly Gln Leu Gln Leu Tyr Arg His Pro Asp Arg
 565 570 575

Ser Gln Pro Ala Phe Leu Asp Ala Ile Asp Arg Arg Glu Asp Thr Phe
 580 585 590

Tyr Val Val Ser Phe Arg Arg Asp His Leu Leu Leu Pro Ala Ile Ser
 595 600 605

His Asn Lys Thr Ser Arg Pro Lys Met Ser Leu Val Met Pro Ala Met
 610 615 620

Ala Pro Asn Glu Thr Leu Ser Gly Arg Gly Ala Pro Gly Asp Tyr Glu
 625 630 635 640

Glu Met Met Gln Ile Glu Cys Glu Val Met Asp Thr Arg Val Ile His
 645 650 655

Ile Lys Thr Ser Thr Val Pro Pro Ser Leu Arg Lys Gln Pro Ser Pro
 660 665 670

Thr Pro Gly Asn Ala Thr Gly Gly Pro Leu Pro Val Ser Ala Ala Ser
 675 680 685

Gln Ala His Gln Ala Ser His Gln Pro Leu Tyr Leu Asn His Pro
 690 695 700

<210> 218

<211> 953

<212> PRT

<213> Homo sapiens

<400> 218

Met Thr Ser Ala Thr Ser Pro Ile Ile Leu Lys Trp Asp Pro Lys Ser
 1 5 10 15

Leu Glu Ile Arg Thr Leu Thr Val Glu Arg Leu Leu Glu Pro Leu Val
 20 25 30

Thr Gln Val Thr Thr Leu Val Asn Thr Ser Asn Lys Gly Pro Ser Gly
 35 40 45

Protein Complexes associated with APP-processing

Lys Lys Lys Gly Arg Ser Lys Lys Ala His Val Leu Ala Ala Ser Val
 50 55 60

Glu Gln Ala Thr Gln Asn Phe Leu Glu Lys Gly Glu Gln Ile Ala Lys
 65 70 75 80

Glu Ser Gln Asp Leu Lys Glu Glu Leu Val Ala Ala Val Glu Asp Val
 85 90 95

Arg Lys Gln Gly Glu Thr Met Arg Ile Ala Ser Ser Glu Phe Ala Asp
 100 105 110

Asp Pro Cys Ser Ser Val Lys Arg Gly Thr Met Val Arg Ala Ala Arg
 115 120 125

Ala Leu Leu Ser Ala Val Thr Arg Leu Leu Ile Leu Ala Asp Met Ala
 130 135 140

Asp Val Met Arg Leu Leu Ser His Leu Lys Ile Val Glu Glu Ala Leu
 145 150 155 160

Glu Ala Val Lys Asn Ala Thr Asn Glu Gln Asp Leu Ala Asn Arg Phe
 165 170 175

Lys Glu Phe Gly Lys Lys Met Val Lys Leu Asn Tyr Val Ala Ala Arg
 180 185 190

Arg Gln Gln Glu Leu Lys Asp Pro His Cys Arg Asp Glu Met Ala Ala
 195 200 205

Ala Arg Gly Ala Leu Lys Lys Asn Ala Thr Met Leu Tyr Thr Ala Ser
 210 215 220

Gln Ala Phe Leu Arg His Pro Asp Val Ala Ala Thr Arg Ala Asn Arg
 225 230 235 240

Asp Tyr Val Phe Lys Gln Val Gln Glu Ala Ile Ala Gly Ile Ser Asn
 245 250 255

Ala Ala Gln Ala Thr Ser Pro Thr Asp Glu Ala Lys Gly His Thr Gly
 260 265 270

Ile Gly Glu Leu Ala Ala Ala Leu Asn Glu Phe Asp Asn Lys Ile Ile
 275 280 285

Leu Asp Pro Met Thr Phe Ser Glu Ala Arg Phe Arg Pro Ser Leu Glu
 290 295 300

Glu Arg Leu Glu Ser Ile Ile Ser Gly Ala Ala Leu Met Ala Asp Ser
 305 310 315 320

Protein Complexes associated with APP-processing

Ser Cys Thr Arg Asp Asp Arg Arg Glu Arg Ile Val Ala Glu Cys Asn
325 330 335

Ala Val Arg Gln Ala Leu Gln Asp Leu Leu Ser Glu Tyr Met Asn Asn
340 345 350

Thr Gly Arg Lys Glu Lys Gly Asp Pro Leu Asn Ile Ala Ile Asp Lys
355 360 365

Met Thr Lys Lys Thr Arg Asp Leu Arg Arg Gln Leu Arg Lys Ala Val
370 375 380

Met Asp His Ile Ser Asp Ser Phe Leu Glu Thr Asn Val Pro Leu Leu
385 390 395 400

Val Leu Ile Glu Ala Ala Lys Ser Gly Asn Glu Lys Glu Val Lys Glu
405 410 415

Tyr Ala Gln Val Phe Arg Glu His Ala Asn Lys Leu Val Glu Val Ala
420 425 430

Asn Leu Ala Cys Ser Ile Ser Asn Asn Glu Glu Gly Val Lys Leu Val
435 440 445

Arg Met Ala Ala Thr Gln Ile Asp Ser Leu Cys Pro Gln Val Ile Asn
450 455 460

Ala Ala Leu Thr Leu Ala Ala Arg Pro Gln Ser Lys Val Ala Gln Asp
465 470 475 480

Asn Met Asp Val Phe Lys Asp Gln Trp Glu Lys Gln Val Arg Val Leu
485 490 495

Thr Glu Ala Val Asp Asp Ile Thr Ser Val Asp Asp Phe Leu Ser Val
500 505 510

Ser Glu Asn His Ile Leu Glu Asp Val Asn Lys Cys Val Ile Ala Leu
515 520 525

Gln Glu Gly Asp Val Asp Thr Leu Asp Arg Thr Ala Gly Ala Ile Arg
530 535 540

Gly Arg Ala Ala Arg Val Ile His Ile Ile Asn Ala Glu Met Glu Asn
545 550 555 560

Tyr Glu Ala Gly Val Tyr Thr Glu Lys Val Leu Glu Ala Thr Lys Leu
565 570 575

Leu Ser Glu Thr Val Met Pro Arg Phe Ala Glu Gln Val Glu Val Ala
580 585 590

Protein Complexes associated with APP-processing
 Ile Glu Ala Leu Ser Ala Asn Val Pro Gln Pro Phe Glu Glu Asn Glu
 595 600 605

Phe Ile Asp Ala Ser Arg Leu Val Tyr Asp Gly Val Arg Asp Ile Arg
 610 615 620

Lys Ala Val Leu Met Ile Arg Thr Pro Glu Glu Leu Glu Asp Asp Ser
 625 630 635 640

Asp Phe Glu Gln Glu Asp Tyr Asp Val Arg Arg Gly Thr Ser Val Gln
 645 650 655

Thr Glu Asp Asp Gln Leu Ile Ala Gly Gln Ser Ala Arg Ala Ile Met
 660 665 670

Ala Gln Leu Pro Gln Glu Glu Lys Ala Lys Ile Ala Glu Gln Val Glu
 675 680 685

Ile Phe His Gln Glu Lys Ser Lys Leu Asp Ala Glu Val Ala Lys Trp
 690 695 700

Asp Asp Ser Gly Asn Asp Ile Ile Val Leu Ala Lys Gln Met Cys Met
 705 710 715 720

Ile Met Met Glu Met Thr Asp Phe Thr Arg Gly Lys Gly Pro Leu Lys
 725 730 735

Asn Thr Ser Asp Val Ile Asn Ala Ala Lys Lys Ile Ala Glu Ala Gly
 740 745 750

Ser Arg Met Asp Lys Leu Ala Arg Ala Val Ala Asp Gln Cys Pro Asp
 755 760 765

Ser Ala Cys Lys Gln Asp Leu Leu Ala Tyr Leu Gln Arg Ile Ala Leu
 770 775 780

Tyr Cys His Gln Leu Asn Ile Cys Ser Lys Val Lys Ala Glu Val Gln
 785 790 795 800

Asn Leu Gly Gly Glu Leu Ile Val Ser Gly Thr Gly Val Gln Ser Thr
 805 810 815

Phe Thr Thr Phe Tyr Glu Val Asp Cys Asp Val Ile Asp Gly Gly Arg
 820 825 830

Ala Ser Gln Leu Ser Thr His Leu Pro Thr Cys Ala Glu Gly Ala Pro
 835 840 845

Ile Gly Ser Gly Ser Ser Asp Ser Ser Met Leu Asp Ser Ala Thr Ser
 850 855 860

Protein Complexes associated with APP-processing
 Leu Ile Gln Ala Ala Lys Asn Leu Met Asn Ala Val Val Leu Thr Val
 865 870 875 880

Lys Ala Ser Tyr Val Ala ser Thr Lys Tyr Gln Lys Val Tyr Gly Thr
 885 890 895

Ala Ala Val Asn Ser Pro val Val Ser Trp Lys Met Lys Ala Pro Glu
 900 905 910

Lys Lys Pro Leu Val Lys Arg Glu Lys Pro Glu Glu Phe Gln Thr Arg
 915 920 925

Val Arg Arg Gly Ser Gln Lys Lys His Ile Ser Pro Val Gln Ala Leu
 930 935 940

Ser Glu Phe Lys Ala Met Asp Ser Phe
 945 950

<210> 219

<211> 537

<212> PRT

<213> Homo sapiens

<400> 219

Met Ala Ala Gln Cys Val Thr Lys Val Ala Leu Asn Val Ser Cys Ala
 1 5 10 15

Asn Leu Leu Asp Lys Asp Ile Gly Ser Lys Ser Asp Pro Leu Cys Val
 20 25 30

Leu Phe Leu Asn Thr Ser Gly Gln Gln Trp Tyr Glu Val Glu Arg Thr
 35 40 45

Glu Arg Ile Lys Asn Cys Leu Asn Pro Gln Phe Ser Lys Thr Phe Ile
 50 55 60

Ile Asp Tyr Tyr Phe Glu Val Val Gln Lys Leu Lys Phe Gly Val Tyr
 65 70 75 80

Asp Ile Asp Asn Lys Thr Ile Glu Leu Ser Asp Asp Asp Phe Leu Gly
 85 90 95

Glu Cys Glu Cys Thr Leu Gly Gln Ile Val Ser Ser Lys Lys Leu Thr
 100 105 110

Arg Pro Leu Val Met Lys Thr Gly Arg Pro Ala Gly Lys Gly Ser Ile
 115 120 125

Protein Complexes associated with APP-processing

Thr Ile Ser Ala Glu Glu Ile Lys Asp Asn Arg Val Val Leu Phe Glu
 130 135 140

Met Glu Ala Arg Lys Leu Asp Asn Lys Asp Leu Phe Gly Lys Ser Asp
 145 150 155 160

Pro Tyr Leu Glu Phe His Lys Gln Thr Ser Asp Gly Asn Trp Leu Met
 165 170 175

Val His Arg Thr Glu Val Val Lys Asn Asn Leu Asn Pro Val Trp Arg
 180 185 190

Pro Phe Lys Ile Ser Leu Asn Ser Leu Cys Tyr Gly Asp Met Asp Lys
 195 200 205

Thr Ile Lys Val Glu Cys Tyr Asp Tyr Asp Asn Asp Gly Ser His Asp
 210 215 220

Leu Ile Gly Thr Phe Gln Thr Thr Met Thr Lys Leu Lys Glu Ala Ser
 225 230 235 240

Arg Ser Ser Pro Val Glu Phe Glu Cys Ile Asn Glu Lys Lys Arg Gln
 245 250 255

Lys Lys Lys Ser Tyr Lys Asn Ser Gly Val Ile Ser Val Lys Gln Cys
 260 265 270

Glu Ile Thr Val Glu Cys Thr Phe Leu Asp Tyr Ile Met Gly Gly Cys
 275 280 285

Gln Leu Asn Phe Thr Val Gly Val Asp Phe Thr Gly Ser Asn Gly Asp
 290 295 300

Pro Arg Ser Pro Asp Ser Leu His Tyr Ile Ser Pro Asn Gly Val Asn
 305 310 315 320

Glu Tyr Leu Thr Ala Leu Trp Ser Val Gly Leu Val Ile Gln Asp Tyr
 325 330 335

Asp Ala Asp Lys Met Phe Pro Ala Phe Gly Phe Gly Ala Gln Ile Pro
 340 345 350

Pro Gln Trp Gln Val Ser His Glu Phe Pro Met Asn Phe Asn Pro Ser
 355 360 365

Asn Pro Tyr Cys Asn Gly Ile Gln Gly Ile Val Glu Ala Tyr Arg Ser
 370 375 380

Cys Leu Pro Gln Ile Lys Leu Tyr Gly Pro Thr Asn Phe Ser Pro Ile
 385 390 395 400

Protein Complexes associated with APP-processing
Ile Asn His Val Ala Arg Phe Ala Ala Ala Ala Thr Gln Gln Gln Thr
405 410 415

Protein Complexes associated with APP-processing

Phe Leu Met Asp Gly Gln Glu Leu Ile Cys Leu Pro Gln Val Phe Asp
85 90 95

Leu Phe Leu Lys His Leu Val Gly Gly Leu His Thr Val Tyr Thr Lys
100 105 110

Leu Lys Arg Leu Asp Ile Ser Pro Val Val Cys Thr Val Glu Gln Val
115 120 125

Arg Ile Leu Arg Gly Leu Gly Ala Ile Gln Pro Gly Val Asn Arg Cys
130 135 140

Lys Leu Ile Thr Arg Lys Asp Phe Glu Thr Leu Phe Thr Asp Cys Thr
145 150 155 160

Asn Ala Arg Arg Lys Arg Gln Met Thr Arg Lys Gln Ala Val Asn Ser
165 170 175

Ser Arg Pro Gly Arg Pro Pro Lys Arg Ser Leu Gly Val Leu Gln Glu
180 185 190

Asn Ala Arg Leu Leu Thr His Ala Val Pro Gly Leu Leu Ser Pro Gly
195 200 205

Leu Ile Thr Pro Thr Gly Ile Thr Ala Ala Ala Met Ala Glu Ala Met
210 215 220

Lys Leu Gln Lys Met Lys Leu Met Ala Met Asn Thr Leu Gln Gly Asn
225 230 235 240

Gly Ser Gln Asn Gly Thr Glu Ser Glu Pro Asp Asp Leu Asn Ser Asn
245 250 255

Thr Gly Gly Ser Glu Ser Ser Trp Asp Lys Asp Lys Met Gln Ser Pro
260 265 270

Phe Ala Ala Pro Gly Pro Gln His Gly Ile Ala His Ala Ala Leu Ala
275 280 285

Gly Gln Pro Gly Ile Gly Gly Ala Pro Thr Leu Asn Pro Leu Gln Gln
290 295 300

Asn His Leu Leu Thr Asn Arg Leu Asp Leu Pro Phe Met Met Met Pro
305 310 315 320

His Pro Leu Leu Pro Val Ser Leu Pro Pro Ala Ser Val Ala Met Ala
325 330 335

Met Asn Gln Met Asn His Leu Asn Thr Ile Ala Asn Met Ala Ala Ala
340 345 350

Protein Complexes associated with APP-processing
 Ala Gln Ile His Ser Pro Leu Ser Arg Ala Gly Thr Ser Val Ile Lys
 355 360 365

Glu Arg Ile Pro Glu Ser Pro Ser Pro Ala Pro Ser Leu Glu Glu Asn
 370 375 380

His Arg Pro Gly Ser Gln Thr Ser Ser His Thr Ser Ser Ser Val Ser
 385 390 395 400

Ser Ser Pro Ser Gln Met Asp His His Leu Glu Arg Met Glu Glu Val
 405 410 415

Pro Val Gln Ile Pro Ile Met Lys Ser Pro Leu Asp Lys Ile Gln Leu
 420 425 430

Thr Pro Gly Gln Ala Leu Pro Ala Gly Phe Pro Gly Pro Phe Ile Phe
 435 440 445

Ala Asp Ser Leu Ser Ser Val Glu Thr Leu Leu Thr Asn Ile Gln Gly
 450 455 460

Leu Leu Lys Val Ala Leu Asp Asn Ala Arg Ile Gln Glu Lys Gln Ile
 465 470 475 480

Gln Gln Glu Lys Lys Glu Leu Arg Leu Glu Leu Tyr Arg Glu Arg Glu
 485 490 495

Ile Arg Glu Asn Leu Glu Arg Gln Leu Ala Val Glu Leu Gln Ser Arg
 500 505 510

Thr Thr Met Gln Lys Arg Leu Lys Lys Glu Lys Lys Thr Lys Arg Lys
 515 520 525

Leu Gln Glu Ala Leu Glu Phe Glu Ser Lys Arg Arg Glu Gln Val Glu
 530 535 540

Gln Ala Leu Lys Gln Ala Thr Thr Ser Asp Ser Gly Leu Arg Met Leu
 545 550 555 560

Lys Asp Thr Gly Ile Pro Asp Ile Glu Ile Glu Asn Asn Gly Thr Pro
 565 570 575

His Asp Ser Ala Ala Met Gln Gly Gly Asn Tyr Tyr Cys Leu Glu Met
 580 585 590

Ala Gln Gln Leu Tyr Ser Ala
 595

<210> 221

<211> 1082

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 221

Met Ala Cys Pro Ala Leu Gly Leu Glu Ala Leu Gln Pro Leu Gln Pro
 1 5 10 15

Glu Pro Pro Pro Glu Pro Ala Phe Ser Glu Ala Gln Lys Trp Ile Glu
 20 25 30

Gln Val Thr Gly Arg Ser Phe Gly Asp Lys Asp Phe Arg Thr Gly Leu
 35 40 45

Glu Asn Gly Ile Leu Leu Cys Glu Leu Leu Asn Ala Ile Lys Pro Gly
 50 55 60

Leu Val Lys Lys Ile Asn Arg Leu Pro Thr Pro Ile Ala Gly Leu Asp
 65 70 75 80

Asn Ile Ile Leu Phe Leu Arg Gly Cys Lys Glu Leu Gly Leu Lys Glu
 85 90 95

Ser Gln Leu Phe Asp Pro Ser Asp Leu Gln Asp Thr Ser Asn Arg Val
 100 105 110

Thr Val Lys Ser Leu Asp Tyr Ser Arg Lys Leu Lys Asn Val Leu Val
 115 120 125

Thr Ile Tyr Trp Leu Gly Lys Ala Ala Asn Ser Cys Thr Ser Tyr Ser
 130 135 140

Gly Thr Thr Leu Asn Leu Lys Glu Phe Glu Gly Leu Leu Ala Gln Met
 145 150 155 160

Arg Lys Asp Thr Asp Asp Ile Glu Ser Pro Lys Arg Ser Ile Arg Asp
 165 170 175

Ser Gly Tyr Ile Asp Cys Trp Asp Ser Glu Arg Ser Asp Ser Leu Ser
 180 185 190

Pro Pro Arg His Gly Arg Asp Asp Ser Phe Asp Ser Leu Asp Ser Phe
 195 200 205

Gly Ser Arg Ser Arg Gln Thr Pro Ser Pro Asp Val Val Leu Arg Gly
 210 215 220

Ser Ser Asp Gly Arg Gly Ser Asp Ser Glu Ser Asp Leu Pro His Arg
 225 230 235 240

Protein Complexes associated with APP-processing

Lys Leu Pro Asp Val Lys Lys Asp Asp Met Ser Ala Arg Arg Thr Ser
245 250 255

His Gly Glu Pro Lys Ser Ala Val Pro Phe Asn Gln Tyr Leu Pro Asn
260 265 270

Lys Ser Asn Gln Thr Ala Tyr Val Pro Ala Pro Leu Arg Lys Lys Lys
275 280 285

Ala Glu Arg Glu Glu Tyr Arg Lys Ser Trp Ser Thr Ala Thr Ser Pro
290 295 300

Leu Gly Gly Glu Arg Pro Phe Arg Tyr Gly Pro Arg Thr Pro Val Ser
305 310 315 320

Asp Asp Ala Glu Ser Thr Ser Met Phe Asp Met Arg Cys Glu Glu Glu
325 330 335

Ala Ala Val Gln Pro His Ser Arg Ala Arg Gln Glu Gln Leu Gln Leu
340 345 350

Ile Asn Asn Gln Leu Arg Glu Glu Asp Asp Lys Trp Gln Asp Asp Leu
355 360 365

Ala Arg Trp Lys Ser Arg Arg Arg Ser Val Ser Gln Asp Leu Ile Lys
370 375 380

Lys Glu Glu Glu Arg Lys Lys Met Glu Lys Leu Leu Ala Gly Glu Asp
385 390 395 400

Gly Thr Ser Glu Arg Arg Lys Ser Ile Lys Thr Tyr Arg Glu Ile Val
405 410 415

Gln Glu Lys Glu Arg Arg Glu Arg Glu Leu His Glu Ala Tyr Lys Asn
420 425 430

Ala Arg Ser Gln Glu Glu Ala Glu Gly Ile Leu Gln Gln Tyr Ile Glu
435 440 445

Arg Phe Thr Ile Ser Glu Ala Val Leu Glu Arg Leu Glu Met Pro Lys
450 455 460

Ile Leu Glu Arg Ser His Ser Thr Glu Pro Asn Leu Ser Ser Phe Leu
465 470 475 480

Asn Asp Pro Asn Pro Met Lys Tyr Leu Arg Gln Gln Ser Leu Pro Pro
485 490 495

Pro Lys Phe Thr Ala Thr Val Glu Thr Thr Ile Ala Arg Ala Ser Val
500 505 510

Protein Complexes associated with APP-processing

Leu Asp Thr Ser Met Ser Ala Gly Ser Gly Ser Pro Ser Lys Thr Val
 515 520 525

Thr Pro Lys Ala Val Pro Met Leu Thr Pro Lys Pro Tyr Ser Gln Pro
 530 535 540

Lys Asn Ser Gln Asp Val Leu Lys Thr Phe Lys Val Asp Gly Lys Val
 545 550 555 560

Ser Val Asn Gly Glu Thr Val His Arg Glu Glu Glu Lys Glu Arg Glu
 565 570 575

Cys Pro Thr Val Ala Pro Ala His Ser Leu Thr Lys Ser Gln Met Phe
 580 585 590

Glu Gly Val Ala Arg Val His Gly Ser Pro Leu Glu Leu Lys Gln Asp
 595 600 605

Asn Gly Ser Ile Glu Ile Asn Ile Lys Lys Pro Asn Ser Val Pro Gln
 610 615 620

Glu Leu Ala Ala Thr Thr Glu Lys Thr Glu Pro Asn Ser Gln Glu Asp
 625 630 635 640

Lys Asn Asp Gly Gly Lys Ser Arg Lys Gly Asn Ile Glu Leu Ala Ser
 645 650 655

Ser Glu Pro Gln His Phe Thr Thr Thr Val Thr Arg Cys Ser Pro Thr
 660 665 670

Val Ala Phe Val Glu Phe Pro Ser Ser Pro Gln Leu Lys Asn Asp Val
 675 680 685

Ser Glu Glu Lys Asp Gln Lys Lys Pro Glu Asn Glu Met Ser Gly Lys
 690 695 700

Val Glu Leu Val Leu Ser Gln Lys Val Val Lys Pro Lys Ser Pro Glu
 705 710 715 720

Pro Glu Ala Thr Leu Thr Phe Pro Phe Leu Asp Lys Met Pro Glu Ala
 725 730 735

Asn Gln Leu His Leu Pro Asn Leu Asn Ser Gln Val Asp Ser Pro Ser
 740 745 750

Ser Glu Lys Ser Pro Val Met Thr Pro Phe Lys Phe Trp Ala Trp Asp
 755 760 765

Pro Glu Glu Glu Arg Arg Arg Gln Glu Lys Trp Gln Gln Glu Gln Glu
 770 775 780

Protein Complexes associated with APP-processing
 Arg Leu Leu Gln Glu Arg Tyr Gln Lys Glu Gln Asp Lys Leu Lys Glu
 785 790 795 800

Glu Trp Glu Lys Ala Gln Lys Glu Val Glu Glu Glu Glu Arg Arg Tyr
 805 810 815

Tyr Glu Glu Glu Arg Lys Ile Ile Glu Asp Thr Val Val Pro Phe Thr
 820 825 830

Val Ser Ser Ser Ser Ala Asp Gln Leu Ser Thr Ser Ser Ser Met Thr
 835 840 845

Glu Gly Ser Gly Thr Met Asn Lys Ile Asp Leu Gly Asn Cys Gln Asp
 850 855 860

Glu Lys Gln Asp Arg Arg Trp Lys Lys Ser Phe Gln Gly Asp Asp Ser
 865 870 875 880

Asp Leu Leu Leu Lys Thr Arg Glu Ser Asp Arg Leu Glu Glu Lys Gly
 885 890 895

Ser Leu Thr Glu Gly Ala Leu Ala His Ser Gly Asn Pro Val Ser Lys
 900 905 910

Gly Val His Glu Asp His Gln Leu Asp Thr Glu Ala Gly Ala Pro His
 915 920 925

Cys Gly Thr Asn Pro Gln Leu Ala Gln Asp Pro Ser Gln Asn Gln Gln
 930 935 940

Thr Ser Asn Pro Thr His Ser Ser Glu Asp Val Lys Pro Lys Thr Leu
 945 950 955 960

Pro Leu Asp Lys Ser Ile Asn His Gln Ile Glu Ser Pro Ser Glu Arg
 965 970 975

Arg Lys Lys Ser Pro Arg Glu His Phe Gln Ala Gly Pro Phe Ser Pro
 980 985 990

Cys Ser Pro Thr Pro Pro Gly Gln Ser Pro Asn Arg Ser Ile Ser Gly
 995 1000 1005

Lys Lys Leu Cys Ser Ser Cys Gly Leu Pro Leu Gly Lys Gly Ala
 1010 1015 1020

Ala Met Ile Ile Glu Thr Leu Asn Leu Tyr Phe His Ile Gln Cys
 1025 1030 1035

Phe Arg Cys Gly Ile Cys Lys Gly Gln Leu Gly Asp Ala Val Ser
 1040 1045 1050

Protein Complexes associated with APP-processing
 Gly Thr Asp Val Arg Ile Arg Asn Gly Leu Leu Asn Cys Asn Asp
 1055 1060 1065

Cys Tyr Met Arg Ser Arg Ser Ala Gly Gln Pro Thr Thr Leu
 1070 1075 1080

<210> 222

<211> 176

<212> PRT

<213> Homo sapiens

<400> 222

Met Ala Ala Arg Gly Arg Arg Ala Glu Pro Gln Gly Arg Glu Ala Pro
 1 5 10 15

Gly Pro Ala Gly Gly Gly Gly Gly Gly Ser Arg Trp Ala Glu Ser Gly
 20 25 30

Ser Gly Thr Ser Pro Glu Ser Gly Asp Glu Glu Val Ser Gly Ala Gly
 35 40 45

Ser Ser Pro Val Ser Gly Gly Val Asn Leu Phe Ala Asn Asp Gly Ser
 50 55 60

Phe Leu Glu Leu Phe Lys Arg Lys Met Glu Glu Glu Gln Arg Gln Arg
 65 70 75 80

Gln Glu Glu Pro Pro Pro Gly Pro Gln Arg Pro Asp Gln Ser Ala Ala
 85 90 95

Ala Ala Gly Pro Gly Asp Pro Lys Arg Lys Gly Gly Pro Gly Ser Thr
 100 105 110

Leu Ser Phe Val Gly Lys Arg Arg Gly Gly Asn Lys Leu Ala Leu Lys
 115 120 125

Thr Gly Ile Val Ala Lys Lys Gln Lys Thr Glu Asp Glu Val Leu Thr
 130 135 140

Ser Lys Gly Asp Ala Trp Ala Lys Tyr Met Ala Glu Val Lys Lys Tyr
 145 150 155 160

Lys Ala His Gln Cys Gly Asp Asp Asp Lys Thr Arg Pro Leu Val Lys
 165 170 175

<210> 223

<211> 1100

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 223

Met Ala Ala Glu Thr Gln Thr Leu Asn Phe Gly Pro Glu Trp Leu Arg
 1 5 10 15

Ala Leu Ser Ser Gly Gly Ser Ile Thr Ser Pro Pro Leu Ser Pro Ala
 20 25 30

Leu Pro Lys Tyr Lys Leu Ala Asp Tyr Arg Tyr Gly Arg Glu Glu Met
 35 40 45

Leu Ala Leu Phe Leu Lys Asp Asn Lys Ile Pro Ser Asp Leu Leu Asp
 50 55 60

Lys Glu Phe Leu Pro Ile Leu Gln Glu Glu Pro Leu Pro Pro Leu Ala
 65 70 75 80

Leu Val Pro Phe Thr Glu Glu Glu Gln Arg Asn Phe Ser Met Ser Val
 85 90 95

Asn Ser Ala Ala Val Leu Arg Leu Thr Gly Arg Gly Gly Gly Gly Thr
 100 105 110

Val Val Gly Ala Pro Arg Gly Arg Ser Ser Ser Arg Gly Arg Gly Arg
 115 120 125

Gly Arg Gly Glu Cys Gly Phe Tyr Gln Arg Ser Phe Asp Glu Val Glu
 130 135 140

Gly Val Phe Gly Arg Gly Gly Gly Arg Glu Met His Arg Ser Gln Ser
 145 150 155 160

Trp Glu Glu Arg Gly Asp Arg Arg Phe Glu Lys Pro Gly Arg Lys Asp
 165 170 175

Val Gly Arg Pro Asn Phe Glu Glu Gly Gly Pro Thr Ser Val Gly Arg
 180 185 190

Lys His Glu Phe Ile Arg Ser Glu Ser Glu Asn Trp Arg Ile Phe Arg
 195 200 205

Glu Glu Gln Asn Gly Glu Asp Glu Asp Gly Gly Trp Arg Leu Ala Gly
 210 215 220

Ser Arg Arg Asp Gly Glu Arg Trp Arg Pro His Ser Pro Asp Gly Pro
 225 230 235 240

Protein Complexes associated with APP-processing

Arg Ser Ala Gly Trp Arg Glu His Met Glu Arg Arg Arg Arg Phe Glu
 245 250 255

Phe Asp Phe Arg Asp Arg Asp Asp Glu Arg Gly Tyr Arg Arg Val Arg
 260 265 270

Ser Gly Ser Gly Ser Ile Asp Asp Asp Arg Asp Ser Leu Pro Glu Trp
 275 280 285

Cys Leu Glu Asp Ala Glu Glu Glu Met Gly Thr Phe Asp Ser Ser Gly
 290 295 300

Ala Phe Leu Ser Leu Lys Lys Val Gln Lys Glu Pro Ile Pro Glu Glu
 305 310 315 320

Gln Glu Met Asp Phe Arg Pro Val Asp Glu Gly Glu Glu Cys Ser Asp
 325 330 335

Ser Glu Gly Ser His Asn Glu Glu Ala Lys Glu Pro Asp Lys Thr Asn
 340 345 350

Lys Lys Glu Gly Glu Lys Thr Asp Arg Val Gly Val Glu Ala Ser Glu
 355 360 365

Glu Thr Pro Gln Thr Ser Ser Ser Ser Ala Arg Pro Gly Thr Pro Ser
 370 375 380

Asp His Gln Ser Gln Glu Ala Ser Gln Phe Glu Arg Lys Asp Glu Pro
 385 390 395 400

Lys Thr Glu Gln Thr Glu Lys Ala Glu Glu Glu Thr Arg Met Glu Asn
 405 410 415

Ser Leu Pro Ala Lys Val Pro Ser Arg Gly Asp Glu Met Val Ala Asp
 420 425 430

Val Gln Gln Pro Leu Ser Gln Ile Pro Ser Asp Thr Ala Ser Pro Leu
 435 440 445

Leu Ile Leu Pro Pro Pro Val Pro Asn Pro Ser Pro Thr Leu Arg Pro
 450 455 460

Val Glu Thr Pro Val Val Gly Ala Pro Gly Met Gly Ser Val Ser Thr
 465 470 475 480

Glu Pro Asp Asp Glu Glu Gly Leu Lys His Leu Glu Gln Gln Ala Glu
 485 490 495

Lys Met Val Ala Tyr Leu Gln Asp Ser Ala Leu Asp Asp Glu Arg Leu
 500 505 510

Protein Complexes associated with APP-processing

Ala Ser Lys₅₁₅ Leu Gln Glu His Arg Ala Lys Gly Val Ser Ile Pro Leu
520 525

Met His₅₃₀ Glu Ala Met Gln Lys₅₃₅ Trp Tyr Tyr Lys Asp₅₄₀ Pro Gln Gly Glu

Ile Gln Gly Pro Phe Asn₅₅₀ Asn Gln Glu Met Ala₅₅₅ Glu Trp Phe Gln Ala₅₆₀

Gly Tyr Phe Thr Met₅₆₅ Ser Leu Leu Val Lys₅₇₀ Arg Ala Cys Asp Glu Ser₅₇₅

Phe Gln Pro Leu₅₈₀ Gly Asp Ile Met Lys₅₈₅ Met Trp Gly Arg Val₅₉₀ Pro Phe

Ser Pro Gly₅₉₅ Pro Ala Pro Pro₆₀₀ His Met Gly Glu Leu Asp Gln Glu₆₀₅

Arg Leu₆₁₀ Thr Arg Gln Gln Glu₆₁₅ Leu Thr Ala Leu Tyr₆₂₀ Gln Met Gln His

Leu Gln Tyr Gln Gln Phe₆₃₀ Leu Ile Gln Gln Gln Tyr Ala Gln Val Leu₆₄₀

Ala Gln Gln Gln Lys₆₄₅ Ala Ala Leu Ser Ser₆₅₀ Gln Gln Gln Gln Gln Leu₆₅₅

Ala Leu Leu Leu₆₆₀ Gln Gln Phe Gln Thr₆₆₅ Leu Lys Met Arg Ile₆₇₀ Ser Asp

Gln Asn Ile₆₇₅ Ile Pro Ser Val Thr₆₈₀ Arg Ser Val Ser Val₆₈₅ Pro Asp Thr

Gly Ser Ile Trp Glu Leu Gln₆₉₅ Pro Thr Ala Ser Gln₇₀₀ Pro Thr Val Trp

Glu Gly Gly Ser Val Trp₇₁₀ Asp Leu Pro Leu Asp₇₁₅ Thr Thr Thr Pro Gly₇₂₀

Pro Ala Leu Glu Gln₇₂₅ Leu Gln Gln Leu Glu₇₃₀ Lys Ala Lys Ala Ala Lys₇₃₅

Leu Glu Gln Glu₇₄₀ Arg Arg Glu Ala Glu₇₄₅ Met Arg Ala Lys Arg Glu Glu₇₅₀

Glu Glu Arg₇₅₅ Lys Arg Gln Glu Glu₇₆₀ Leu Arg Arg Gln Gln Glu Glu Ile₇₆₅

Leu Arg Arg Gln Gln Glu Glu₇₇₀ Glu Arg Lys Arg Arg₇₈₀ Glu Glu Glu Glu

Protein Complexes associated with APP-processing

Leu Ala Arg Arg Lys Gln Glu Glu Ala Leu Arg Arg Gln Arg Glu Gln
 785 790 795 800

Glu Ile Ala Leu Arg Arg Gln Arg Glu Glu Glu Arg Gln Gln Gln
 805 810 815

Glu Glu Ala Leu Arg Arg Leu Glu Glu Arg Arg Arg Glu Glu Glu Glu
 820 825 830

Arg Arg Lys Gln Glu Glu Leu Leu Arg Lys Gln Glu Glu Glu Ala Ala
 835 840 845

Lys Trp Ala Arg Glu Glu Glu Glu Ala Gln Arg Arg Leu Glu Glu Asn
 850 855 860

Arg Leu Arg Met Glu Glu Glu Ala Ala Arg Leu Arg His Glu Glu Glu
 865 870 875 880

Glu Arg Lys Arg Lys Glu Leu Glu Val Gln Arg Gln Lys Glu Leu Met
 885 890 895

Arg Gln Arg Gln Gln Gln Gln Glu Ala Leu Arg Arg Leu Gln Gln Gln
 900 905 910

Gln Gln Gln Gln Gln Leu Ala Gln Met Lys Leu Pro Ser Ser Ser Thr
 915 920 925

Trp Gly Gln Gln Ser Asn Thr Thr Ala Cys Gln Ser Gln Ala Thr Leu
 930 935 940

Ser Leu Ala Glu Ile Gln Lys Leu Glu Glu Glu Arg Glu Arg Gln Leu
 945 950 955 960

Arg Glu Glu Gln Arg Arg Gln Gln Arg Glu Leu Met Lys Ala Leu Gln
 965 970 975

Gln Gln Gln Gln Gln Gln Gln Gln Lys Leu Ser Gly Trp Gly Asn Val
 980 985 990

Ser Lys Pro Ser Gly Thr Thr Lys Ser Leu Leu Glu Ile Gln Gln Glu
 995 1000 1005

Glu Ala Arg Gln Met Gln Lys Gln Gln Gln Gln Gln Gln His
 1010 1015 1020

Gln Gln Pro Asn Arg Ala Arg Asn Asn Thr His Ser Asn Leu His
 1025 1030 1035

Thr Ser Ile Gly Asn Ser Val Trp Gly Ser Ile Asn Thr Gly Pro
 1040 1045 1050

Protein Complexes associated with APP-processing
 Pro Asn Gln Trp Ala Ser Asp Leu Val Ser Ser Ile Trp Ser Asn
 1055 1060 1065

Ala Asp Thr Lys Asn Ser Asn Met Gly Phe Trp Asp Asp Ala Val
 1070 1075 1080

Lys Glu Val Gly Pro Arg Asn Ser Thr Asn Lys Asn Lys Lys Glu
 1085 1090 1095

Leu Lys
 1100

<210> 224

<211> 370

<212> PRT

<213> Homo sapiens

<400> 224

Met Val Gly Lys Leu Lys Gln Asn Leu Leu Leu Ala Cys Leu Val Ile
 1 5 10 15

Ser Ser Val Thr Val Phe Tyr Leu Gly Gln His Ala Met Glu Cys His
 20 25 30

His Arg Ile Glu Glu Arg Ser Gln Pro Val Lys Leu Glu Ser Thr Arg
 35 40 45

Thr Thr Val Arg Thr Gly Leu Asp Leu Lys Ala Asn Lys Thr Phe Ala
 50 55 60

Tyr His Lys Asp Met Pro Leu Ile Phe Ile Gly Gly Val Pro Arg Ser
 65 70 75 80

Gly Thr Thr Leu Met Arg Ala Met Leu Asp Ala His Pro Asp Ile Arg
 85 90 95

Cys Gly Glu Glu Thr Arg Val Ile Pro Arg Ile Leu Ala Leu Lys Gln
 100 105 110

Met Trp Ser Arg Ser Ser Lys Glu Lys Ile Arg Leu Asp Glu Ala Gly
 115 120 125

Val Thr Asp Glu Val Leu Asp Ser Ala Met Gln Ala Phe Leu Leu Glu
 130 135 140

Ile Ile Val Lys His Gly Glu Pro Ala Pro Tyr Leu Cys Asn Lys Asp
 145 150 155 160

Protein Complexes associated with APP-processing
 Pro Phe Ala Leu Lys Ser Leu Thr Tyr Leu Ser Arg Leu Phe Pro Asn
 165 170 175

Ala Lys Phe Leu Leu Met Val Arg Asp Gly Arg Ala Ser Val His Ser
 180 185 190

Met Ile Ser Arg Lys Val Thr Ile Ala Gly Phe Asp Leu Asn Ser Tyr
 195 200 205

Arg Asp Cys Leu Thr Lys Trp Asn Arg Ala Ile Glu Thr Met Tyr Asn
 210 215 220

Gln Cys Met Glu Val Gly Tyr Lys Lys Cys Met Leu Val His Tyr Glu
 225 230 235 240

Gln Leu Val Leu His Pro Glu Arg Trp Met Arg Thr Leu Leu Lys Phe
 245 250 255

Leu Gln Ile Pro Trp Asn His Ser Val Leu His His Glu Glu Met Ile
 260 265 270

Gly Lys Ala Gly Gly Val Ser Leu Ser Lys Val Glu Arg Ser Thr Asp
 275 280 285

Gln Val Ile Lys Pro Val Asn Val Gly Ala Leu Ser Lys Trp Val Gly
 290 295 300

Lys Ile Pro Pro Asp Val Leu Gln Asp Met Ala Val Ile Ala Pro Met
 305 310 315 320

Leu Ala Lys Leu Gly Tyr Asp Pro Tyr Ala Asn Pro Pro Asn Tyr Gly
 325 330 335

Lys Pro Asp Pro Lys Ile Ile Glu Asn Thr Arg Arg Val Tyr Lys Gly
 340 345 350

Glu Phe Gln Leu Pro Asp Phe Leu Lys Glu Lys Pro Gln Thr Glu Gln
 355 360 365

Val Glu
 370

<210> 225

<211> 454

<212> PRT

<213> Homo sapiens

<400> 225

Protein Complexes associated with APP-processing

Met Ser Thr Phe Arg Gln Glu Asp Val Glu Asp His Tyr Glu Met Gly
 1 5 10 15

Glu Glu Leu Gly Ser Gly Gln Phe Ala Ile Val Arg Lys Cys Arg Gln
 20 25 30

Lys Gly Thr Gly Lys Glu Tyr Ala Ala Lys Phe Ile Lys Lys Arg Arg
 35 40 45

Leu Ser Ser Ser Arg Arg Gly Val Ser Arg Glu Glu Ile Glu Arg Glu
 50 55 60

Val Asn Ile Leu Arg Glu Ile Arg His Pro Asn Ile Ile Thr Leu His
 65 70 75 80

Asp Ile Phe Glu Asn Lys Thr Asp Val Val Leu Ile Leu Glu Leu Val
 85 90 95

Ser Gly Gly Glu Leu Phe Asp Phe Leu Ala Glu Lys Glu Ser Leu Thr
 100 105 110

Glu Asp Glu Ala Thr Gln Phe Leu Lys Gln Ile Leu Asp Gly Val His
 115 120 125

Tyr Leu His Ser Lys Arg Ile Ala His Phe Asp Leu Lys Pro Glu Asn
 130 135 140

Ile Met Leu Leu Asp Lys Asn Val Pro Asn Pro Arg Ile Lys Leu Ile
 145 150 155 160

Asp Phe Gly Ile Ala His Lys Ile Glu Ala Gly Asn Glu Phe Lys Asn
 165 170 175

Ile Phe Gly Thr Pro Glu Phe Val Ala Pro Glu Ile Val Asn Tyr Glu
 180 185 190

Pro Leu Gly Leu Glu Ala Asp Met Trp Ser Ile Gly Val Ile Thr Tyr
 195 200 205

Ile Leu Leu Ser Gly Ala Ser Pro Phe Leu Gly Glu Thr Lys Gln Glu
 210 215 220

Thr Leu Thr Asn Ile Ser Ala Val Asn Tyr Asp Phe Asp Glu Glu Tyr
 225 230 235 240

Phe Ser Asn Thr Ser Glu Leu Ala Lys Asp Phe Ile Arg Arg Leu Leu
 245 250 255

Val Lys Asp Pro Lys Arg Arg Met Thr Ile Ala Gln Ser Leu Glu His
 260 265 270

Protein Complexes associated with APP-processing
 Ser Trp Ile Lys Ala Ile Arg Arg Asn Val Arg Gly Glu Asp Ser
 275 280 285

Gly Arg Lys Pro Glu Arg Arg Arg Leu Lys Thr Thr Arg Leu Lys Glu
 290 295 300

Tyr Thr Ile Lys Ser His Ser Ser Leu Pro Pro Asn Asn Ser Tyr Ala
 305 310 315 320

Asp Phe Glu Arg Phe Ser Lys Val Leu Glu Glu Ala Ala Ala Ala Glu
 325 330 335

Glu Gly Leu Arg Glu Leu Gln Arg Ser Arg Arg Leu Cys His Glu Asp
 340 345 350

Val Glu Ala Leu Ala Ala Ile Tyr Glu Glu Lys Glu Ala Trp Tyr Arg
 355 360 365

Glu Glu Ser Asp Ser Leu Gly Gln Asp Leu Arg Arg Leu Arg Gln Glu
 370 375 380

Leu Leu Lys Thr Glu Ala Leu Lys Arg Gln Ala Gln Glu Glu Ala Lys
 385 390 395 400

Gly Ala Leu Leu Gly Thr Ser Gly Leu Lys Arg Arg Phe Ser Arg Leu
 405 410 415

Glu Asn Arg Tyr Glu Ala Leu Ala Lys Gln Val Ala Ser Glu Met Arg
 420 425 430

Phe Val Gln Asp Leu Val Arg Ala Leu Glu Gln Glu Lys Leu Gln Gly
 435 440 445

Val Glu Cys Gly Leu Arg
 450

<210> 226

<211> 255

<212> PRT

<213> Homo sapiens

<400> 226

Met Ala Phe Arg Gln Ala Leu Gln Leu Ala Ala Cys Gly Leu Ala Gly
 1 5 10 15

Gly Ser Ala Ala Val Leu Phe Ser Ala Val Ala Val Gly Lys Pro Arg
 20 25 30

Protein Complexes associated with APP-processing
 Ala Gly Gly Asp Ala Glu Pro Arg Pro Ala Glu Pro Pro Ala Trp Ala
 35 40 45

Gly Gly Ala Arg Pro Gly Pro Gly Val Trp Asp Pro Asn Trp Asp Arg
 50 55 60

Arg Glu Pro Leu Ser Leu Ile Asn Val Arg Lys Arg Asn Val Glu Ser
 65 70 75 80

Gly Glu Glu Glu Leu Ala Ser Lys Leu Asp His Tyr Lys Ala Lys Ala
 85 90 95

Thr Arg His Ile Phe Leu Ile Arg His Ser Gln Tyr His Val Asp Gly
 100 105 110

Ser Leu Glu Lys Asp Arg Thr Leu Thr Pro Leu Gly Arg Glu Gln Ala
 115 120 125

Glu Leu Thr Gly Leu Arg Leu Ala Ser Leu Gly Leu Lys Phe Asn Lys
 130 135 140

Ile Val His Ser Ser Met Thr Arg Ala Ile Glu Thr Thr Asp Ile Ile
 145 150 155 160

Ser Arg His Leu Pro Gly Val Cys Lys Val Ser Thr Asp Leu Leu Arg
 165 170 175

Glu Gly Ala Pro Ile Glu Pro Asp Pro Pro Val Ser His Trp Lys Pro
 180 185 190

Glu Ala Val Gln Tyr Tyr Glu Asp Gly Ala Arg Ile Glu Ala Ala Phe
 195 200 205

Arg Asn Tyr Ile His Arg Ala Asp Ala Arg Gln Glu Glu Asp Ser Tyr
 210 215 220

Glu Ile Phe Ile Cys His Ala Asn Val Ile Arg Tyr Ile Val Cys Ser
 225 230 235 240

Ile Pro Pro Leu Leu Ser Ala Gly Asp Phe Val Val Leu Gly Ser
 245 250 255

<210> 227

<211> 189

<212> PRT

<213> Homo sapiens

<400> 227

Protein Complexes associated with APP-processing
 Met Ser Glu Asp Asn Arg Pro Leu Thr Gly Leu Ala Ala Ala Ile Ala
 1 5 10 15

Gly Ala Lys Leu Arg Lys Val Ser Arg Met Glu Asp Thr Ser Phe Pro
 20 25 30

Ser Gly Gly Asn Ala Ile Gly Val Asn Ser Ala Ser Ser Lys Thr Asp
 35 40 45

Thr Gly Arg Gly Asn Gly Pro Leu Pro Leu Gly Gly Ser Gly Leu Met
 50 55 60

Glu Glu Met Ser Ala Leu Leu Ala Arg Arg Arg Arg Ile Ala Glu Lys
 65 70 75 80

Gly Ser Thr Ile Glu Thr Glu Gln Lys Glu Asp Lys Gly Glu Asp Ser
 85 90 95

Glu Pro Val Thr Ser Lys Ala Ser Ser Thr Ser Thr Pro Glu Pro Thr
 100 105 110

Arg Lys Pro Trp Glu Arg Thr Asn Thr Met Asn Gly Ser Lys Ser Pro
 115 120 125

Val Ile Ser Arg Pro Lys Ser Thr Pro Leu Ser Gln Pro Ser Ala Asn
 130 135 140

Gly Val Gln Thr Glu Gly Leu Asp Tyr Asp Arg Leu Lys Gln Asp Ile
 145 150 155 160

Leu Asp Glu Met Arg Lys Glu Leu Thr Lys Leu Lys Glu Glu Leu Ile
 165 170 175

Asp Ala Ile Arg Gln Glu Leu Ser Lys Ser Asn Thr Ala
 180 185

<210> 228

<211> 730

<212> PRT

<213> Homo sapiens

<400> 228

Arg His Thr Arg Thr His Arg Asp Thr Arg His Thr Tyr Thr His Ala
 1 5 10 15

His Thr Asp Ala His Thr Cys Thr His Met His Arg Asp Thr Gln Met
 20 25 30

Protein Complexes associated with APP-processing

His Thr His Thr Ile Cys Arg Lys Lys Tyr Ala Leu Thr Asn Ile Gln
 35 40 45

Ala Ala Met Gly Leu Ser Asp Pro Ala Ala Gln Pro Leu Leu Gly Asn
 50 55 60

Gly Ser Ala Asn Ile Lys Leu Val Lys Asn Gly Glu Asn Gln Leu Arg
 65 70 75 80

Lys Ala Ala Glu Gln Gly Gln Gln Asp Pro Asn Lys Asn Leu Ser Pro
 85 90 95

Thr Ala Val Ile Asn Ile Thr Ser Glu Lys Leu Glu Gly Lys Glu Pro
 100 105 110

His Pro Gln Asp Ser Ser Ser Cys Glu Ile Leu Pro Ser Gln Pro Arg
 115 120 125

Arg Thr Lys Ser Phe Leu Asn Tyr Tyr Ala Asp Leu Glu Thr Ser Ala
 130 135 140

Arg Glu Leu Glu Gln Asn Arg Gly Asn His His Gly Thr Ala Glu Glu
 145 150 155 160

Lys Ser Gln Pro Val Gln Gly Gln Ala Ser Thr Ile Ile Gly Asn Gly
 165 170 175

Asp Leu Leu Leu Gln Lys Pro Asn Arg Pro Gln Ser Ser Pro Glu Asp
 180 185 190

Gly Gln Val Ala Thr Val Ser Ser Ser Pro Glu Thr Lys Lys Asp His
 195 200 205

Pro Lys Thr Gly Ala Lys Thr Asp Cys Ala Leu His Arg Ile Gln Asn
 210 215 220

Leu Ala Pro Ser Asp Glu Glu Ser Ser Trp Thr Thr Leu Ser Gln Asp
 225 230 235 240

Ser Ala Ser Pro Ser Ser Pro Asp Glu Thr Asp Ile Trp Ser Asp His
 245 250 255

Ser Phe Gln Thr Asp Pro Asp Leu Pro Pro Gly Trp Lys Arg Val Ser
 260 265 270

Asp Ile Ala Gly Thr Tyr Tyr Trp His Ile Pro Thr Gly Thr Thr Gln
 275 280 285

Trp Glu Arg Pro Val Ser Ile Pro Ala Asp Leu Gln Gly Ser Arg Lys
 290 295 300

Protein Complexes associated with APP-processing

Gly Ser Leu Ser Ser Val Thr Pro Ser Pro Thr Pro Glu Asn Glu Lys
 305 310 315 320

Gln Pro Trp Ser Asp Phe Ala Val Leu Asn Gly Gly Lys Ile Asn Ser
 325 330 335

Asp Ile Trp Lys Asp Leu His Ala Ala Thr Val Asn Pro Asp Pro Ser
 340 345 350

Leu Lys Glu Phe Glu Gly Ala Thr Leu Arg Tyr Ala Ser Leu Lys Leu
 355 360 365

Arg Asn Ala Pro His Pro Asp Asp Asp Asp Ser Cys Ser Ile Asn Ser
 370 375 380

Asp Pro Glu Ala Lys Cys Phe Ala Val Arg Ser Leu Gly Trp Val Glu
 385 390 395 400

Met Ala Glu Glu Asp Leu Ala Pro Gly Lys Ser Ser Val Ala Val Asn
 405 410 415

Asn Cys Ile Arg Gln Leu Ser Tyr Cys Lys Asn Asp Ile Arg Asp Thr
 420 425 430

Val Gly Ile Trp Gly Glu Gly Lys Asp Met Tyr Leu Ile Leu Glu Asn
 435 440 445

Asp Met Leu Ser Leu Val Asp Pro Met Asp Arg Ser Val Trp His Ser
 450 455 460

Gln Pro Ile Val Ser Ile Arg Val Trp Gly Val Gly Arg Asp Asn Gly
 465 470 475 480

Arg Asp Phe Ala Tyr Val Ala Arg Asp Lys Asp Thr Arg Ile Leu Lys
 485 490 495

Cys His Val Phe Arg Cys Asp Thr Pro Ala Lys Ala Ile Ala Thr Ser
 500 505 510

Leu His Glu Ile Cys Ser Lys Ile Met Ala Glu Arg Lys Asn Ala Lys
 515 520 525

Ala Leu Ala Cys Ser Ser Leu Gln Glu Arg Ala Asn Val Asn Leu Asp
 530 535 540

Val Pro Leu Gln Val Asp Phe Pro Thr Pro Lys Thr Glu Leu Val Gln
 545 550 555 560

Lys Phe His Val Gln Tyr Leu Gly Met Leu Pro Val Asp Lys Pro Val
 565 570 575

Protein Complexes associated with APP-processing

Protein Complexes associated with APP-processing

Asn Lys Glu Asp Trp Leu Ser Val Asn Met Asn Val Ala Asp Ala Thr
595 600 605

Val Thr Val Ile Ser Glu Lys Asn Glu Glu Glu Val Leu Val Glu Cys
610 615 620

Arg Val Arg Phe Leu Ser Phe Met Gly Val Gly Lys Asp Val His Thr
625 630 635 640

Phe Ala Phe Ile Met Asp Thr Gly Asn Gln Arg Phe Glu Cys His Val
645 650 655

Phe Trp Cys Glu Pro Asn Ala Gly Asn Val Ser Glu Ala Val Gln Ala
660 665 670

Ala Cys Met Leu Arg Tyr Gln Lys Cys Leu Val Ala Arg Pro Pro Ser
675 680 685

Gln Lys Val Arg Pro Pro Pro Pro Ala Asp Ser Val Thr Arg Arg
690 695 700

Val Thr Thr Asn Val Lys Arg Gly Val Leu Ser Leu Ile Asp Thr Leu
705 710 715 720

Lys Gln Lys Arg Pro Val Thr Glu Met Pro
725 730

<210> 229

<211> 711

<212> PRT

<213> Homo sapiens

<400> 229

Met Ala Glu Arg Glu Ser Gly Gly Leu Gly Gly Gly Ala Ala Ser Pro
1 5 10 15

Pro Ala Ala Ser Pro Phe Leu Gly Leu His Ile Ala Ser Pro Pro Asn
20 25 30

Phe Arg Leu Thr His Asp Ile Ser Leu Glu Glu Phe Glu Asp Glu Asp

Leu Ser Glu Ile Thr Asp Glu Cys Gly Ile Ser Leu Gln Cys Lys Asp
50 55 60

Protein Complexes associated with APP-processing

Thr Leu Ser Leu Arg Pro Pro Arg Ala Gly Leu Leu Ser Ala Gly Gly
 65 70 75 80
 Gly Gly Ala Gly Ser Arg Leu Gln Ala Glu Met Leu Gln Met Asp Leu
 85 90 95
 Ile Asp Ala Thr Gly Asp Thr Pro Gly Ala Glu Asp Asp Glu Glu Asp
 100 105 110
 Asp Asp Glu Glu Arg Ala Ala Arg Arg Pro Gly Ala Gly Pro Pro Lys
 115 120 125
 Ala Glu Ser Gly Gln Glu Pro Ala Ser Arg Gly Gln Gly Gln Ser Gln
 130 135 140
 Gly Gln Ser Gln Gly Pro Gly Ser Gly Asp Thr Tyr Arg Pro Lys Arg
 145 150 155 160
 Pro Thr Thr Leu Asn Leu Phe Pro Gln Val Pro Arg Ser Gln Asp Thr
 165 170 175
 Leu Asn Asn Asn Ser Leu Gly Lys Lys His Ser Trp Gln Asp Arg Val
 180 185 190
 Ser Arg Ser Ser Ser Pro Leu Lys Thr Gly Glu Gln Thr Pro Pro His
 195 200 205
 Glu His Ile Cys Leu Ser Asp Glu Leu Pro Pro Gln Ser Gly Pro Ala
 210 215 220
 Pro Thr Thr Asp Arg Gly Thr Ser Thr Asp Ser Pro Cys Arg Arg Ser
 225 230 235 240
 Thr Ala Thr Gln Met Ala Pro Pro Gly Gly Pro Pro Ala Ala Pro Pro
 245 250 255
 Gly Gly Arg Gly His Ser His Arg Asp Arg Ile His Tyr Gln Ala Asp
 260 265 270
 Val Arg Leu Glu Ala Thr Glu Glu Ile Tyr Leu Thr Pro Val Gln Arg
 275 280 285
 Pro Pro Asp Ala Ala Glu Pro Thr Ser Ala Phe Leu Pro Pro Thr Glu
 290 295 300
 Ser Arg Met Ser Val Ser Ser Asp Pro Asp Pro Ala Ala Tyr Pro Ser
 305 310 315 320
 Thr Ala Gly Arg Pro His Pro Ser Ile Ser Glu Glu Glu Glu Gly Phe
 325 330 335

Protein Complexes associated with APP-processing

Ile Ala Thr Thr Arg Arg Leu Thr Val His Phe Asn Pro Pro Ser Ser
595 600 605

Protein Complexes associated with APP-processing

Cys Val Leu Glu Ile Ser Val Arg Gly Val Lys Ile Gly Val Lys Ala
 610 615 620

Asp Asp Ser Gln Glu Ala Lys Gly Asn Lys Cys Ser His Phe Phe Gln
 625 630 635 640

Leu Lys Asn Ile Ser Phe Cys Gly Tyr His Pro Lys Asn Asn Lys Tyr
 645 650 655

Phe Gly Phe Ile Thr Lys His Pro Ala Asp His Arg Phe Ala Cys His
 660 665 670

Val Phe Val Ser Glu Asp Ser Thr Lys Ala Leu Ala Glu Ser Val Gly
 675 680 685

Arg Ala Phe Gln Gln Phe Tyr Lys Gln Phe Val Glu Tyr Thr Cys Pro
 690 695 700

Thr Glu Asp Ile Tyr Leu Glu
 705 710

<210> 230

<211> 93

<212> PRT

<213> Homo sapiens

<400> 230

Gly Ser Glu Leu Glu Thr Ala Met Glu Thr Leu Ile Asn Val Phe His
 1 5 10 15

Ala His Ser Gly Lys Glu Gly Asp Lys Tyr Lys Leu Ser Lys Lys Glu
 20 25 30

Leu Lys Glu Leu Leu Gln Thr Glu Leu Ser Gly Phe Leu Asp Ala Gln
 35 40 45

Lys Asp Val Asp Ala Val Asp Lys Val Met Lys Glu Leu Asp Glu Asn
 50 55 60

Gly Asp Gly Glu Val Asp Phe Gln Glu Tyr Val Val Leu Val Ala Ala
 65 70 75 80

Leu Thr Val Ala Cys Asn Asn Phe Phe Trp Glu Asn Ser
 85 90

<210> 231

<211> 91

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 231

Ser Glu Leu Glu Lys Ala Met Val Ala Leu Ile Asp Val Phe His Gln
 1 5 10 15

Tyr Ser Gly Arg Glu Gly Asp Lys His Lys Leu Lys Lys Ser Glu Leu
 20 25 30

Lys Glu Leu Ile Asn Asn Glu Leu Ser His Phe Leu Glu Glu Ile Lys
 35 40 45

Glu Gln Glu Val Val Asp Lys Val Met Glu Thr Leu Asp Asn Asp Gly
 50 55 60

Asp Gly Glu Cys Asp Phe Gln Glu Phe Met Ala Phe Val Ala Met Val
 65 70 75 80

Thr Thr Ala Cys His Glu Phe Phe Glu His Glu
 85 90

<210> 232

<211> 695

<212> PRT

<213> Homo sapiens

<400> 232

Met Leu Pro Gly Leu Ala Leu Leu Leu Leu Ala Ala Trp Thr Ala Arg
 1 5 10 15

Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro
 20 25 30

Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
 35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
 50 55 60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
 85 90 95

Protein Complexes associated with APP-processing
 Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
 100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
 165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
 180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
 210 215 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
 225 230 235 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
 245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
 260 265 270

Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
 275 280 285

Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
 290 295 300

Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
 305 310 315 320

Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
 325 330 335

Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
 340 345 350

Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
 355 360 365

Protein Complexes associated with APP-processing
 Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
 370 375 380

Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
 385 390 395 400

Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
 405 410 415

Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
 420 425 430

Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
 435 440 445

Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
 450 455 460

Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
 465 470 475 480

Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
 485 490 495

Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
 500 505 510

Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
 515 520 525

Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
 530 535 540

Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn
 545 550 555 560

Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
 565 570 575

Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
 580 585 590

Glu Val Asn Leu Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
 595 600 605

His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
 610 615 620

Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
 625 630 635 640

Protein Complexes associated with APP-processing
 Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
 645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
 660 665 670

His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
 675 680 685

Phe Phe Glu Gln Met Gln Asn
 690 695

<210> 233

<211> 383

<212> PRT

<213> Homo sapiens

<400> 233

Met Thr Ala Thr Glu Ala Leu Leu Arg Val Leu Leu Leu Leu Leu Ala
 1 5 10 15

Phe Gly His Ser Thr Tyr Gly Ala Glu Cys Phe Pro Ala Cys Asn Pro
 20 25 30

Gln Asn Gly Phe Cys Glu Asp Asp Asn Val Cys Arg Cys Gln Pro Gly
 35 40 45

Trp Gln Gly Pro Leu Cys Asp Gln Cys Val Thr Ser Pro Gly Cys Leu
 50 55 60

His Gly Leu Cys Gly Glu Pro Gly Gln Cys Ile Cys Thr Asp Gly Trp
 65 70 75 80

Asp Gly Glu Leu Cys Asp Arg Asp Val Arg Ala Cys Ser Ser Ala Pro
 85 90 95

Cys Ala Asn Asn Gly Thr Cys Val Ser Leu Asp Gly Gly Leu Tyr Glu
 100 105 110

Cys Ser Cys Ala Pro Gly Tyr Ser Gly Lys Asp Cys Gln Lys Lys Asp
 115 120 125

Gly Pro Cys Val Ile Asn Gly Ser Pro Cys Gln His Gly Gly Thr Cys
 130 135 140

Val Asp Asp Glu Gly Arg Ala Ser His Ala Ser Cys Leu Cys Pro Pro
 145 150 155 160

Protein Complexes associated with APP-processing
 Gly Phe Ser Gly Asn Phe Cys Glu Ile Val Ala Asn Ser Cys Thr Pro
 165 170 175

Asn Pro Cys Glu Asn Asp Gly Val Cys Thr Asp Ile Gly Gly Asp Phe
 180 185 190

Arg Cys Arg Cys Pro Ala Gly Phe Ile Asp Lys Thr Cys Ser Arg Pro
 195 200 205

Val Thr Asn Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Thr Cys Leu
 210 215 220

Gln His Thr Gln Val Ser Tyr Glu Cys Leu Cys Lys Pro Glu Phe Thr
 225 230 235 240

Gly Leu Thr Cys Val Lys Lys Arg Ala Leu Ser Pro Gln Gln Val Thr
 245 250 255

Arg Leu Pro Ser Gly Tyr Gly Leu Ala Tyr Arg Leu Thr Pro Gly Val
 260 265 270

His Glu Leu Pro Val Gln Gln Pro Glu His Arg Ile Leu Lys Val Ser
 275 280 285

Met Lys Glu Leu Asn Lys Lys Thr Pro Leu Leu Thr Glu Gly Gln Ala
 290 295 300

Ile Cys Phe Thr Ile Leu Gly Val Leu Thr Ser Leu Val Val Leu Gly
 305 310 315 320

Thr Val Gly Ile Val Phe Leu Asn Lys Cys Glu Thr Trp Val Ser Asn
 325 330 335

Leu Arg Tyr Asn His Met Leu Arg Lys Lys Lys Asn Leu Leu Leu Gln
 340 345 350

Tyr Asn Ser Gly Glu Asp Leu Ala Val Asn Ile Ile Phe Pro Glu Lys
 355 360 365

Ile Asp Met Thr Thr Phe Ser Lys Glu Ala Gly Asp Glu Glu Ile
 370 375 380

<210> 234

<211> 283

<212> PRT

<213> Homo sapiens

<400> 234

Protein Complexes associated with APP-processing

Met Val Asn Tyr Ala Trp Ala Gly Arg Ser Gln Arg Lys Leu Trp Trp
 1 5 10 15

Arg Ser Val Ala Val Leu Thr Cys Lys Ser Val Val Arg Pro Gly Tyr
 20 25 30

Arg Gly Gly Leu Gln Ala Arg Arg Ser Thr Leu Leu Lys Thr Cys Ala
 35 40 45

Arg Ala Arg Ala Thr Ala Pro Gly Ala Met Lys Met Val Ala Pro Trp
 50 55 60

Thr Arg Phe Tyr Ser Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr
 65 70 75 80

Gly Thr Ile Leu Leu Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val
 85 90 95

Leu Leu Ile Leu Leu Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe
 100 105 110

Ser Ser Ser Glu Leu Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn
 115 120 125

Met Cys Ile Ala Ile Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala
 130 135 140

Met Ala Thr Tyr Gly Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro
 145 150 155 160

Phe Phe Cys Tyr Gln Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala
 165 170 175

Ile Thr Val Leu Ile Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln
 180 185 190

Leu Pro Pro Asn Phe Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro
 195 200 205

Thr Cys Leu Val Leu Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr
 210 215 220

Phe Lys Gly Tyr Leu Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile
 225 230 235 240

Asn Gly Arg Asn Ser Ser Asp Val Leu Val Tyr Val Thr Ser Asn Asp
 245 250 255

Thr Thr Val Leu Leu Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala
 260 265 270

Protein Complexes associated with APP-processing
 Ala Lys Glu Pro Pro Pro Pro Tyr Val Ser Ala
 275 280

<210> 235

<211> 613

<212> .PRT

<213> Homo sapiens

<400> 235

Met Ala Thr Ile Pro Asp Trp Lys Leu Gln Leu Leu Ala Arg Arg Arg
 1 5 10 15

Gln Glu Glu Ala Ser Val Arg Gly Arg Glu Lys Ala Glu Arg Glu Arg
 20 25 30

Leu Ser Gln Met Pro Ala Trp Lys Arg Gly Leu Leu Glu Arg Arg Arg
 35 40 45

Ala Lys Leu Gly Leu Ser Pro Gly Glu Pro Ser Pro Val Leu Gly Thr
 50 55 60

Val Glu Ala Gly Pro Pro Asp Pro Asp Glu Ser Ala Val Leu Leu Glu
 65 70 75 80

Ala Ile Gly Pro Val His Gln Asn Arg Phe Ile Arg Gln Glu Arg Gln
 85 90 95

Gln Gln Gln Gln Gln Gln Gln Arg Ser Glu Glu Leu Leu Ala Glu Arg
 100 105 110

Lys Pro Gly Pro Leu Glu Ala Arg Glu Arg Arg Pro Ser Pro Gly Glu
 115 120 125

Met Arg Asp Gln Ser Pro Lys Gly Arg Glu Ser Arg Glu Glu Arg Leu
 130 135 140

Ser Pro Arg Glu Thr Arg Glu Arg Arg Leu Gly Ile Gly Gly Ala Gln
 145 150 155 160

Glu Leu Ser Leu Arg Pro Leu Glu Ala Arg Asp Trp Arg Gln Ser Pro
 165 170 175

Gly Glu Val Gly Asp Arg Ser Ser Arg Leu Ser Glu Ala Trp Lys Trp
 180 185 190

Arg Leu Ser Pro Gly Glu Thr Pro Glu Arg Ser Leu Arg Leu Ala Glu
 195 200 205

Protein Complexes associated with APP-processing

Ser Arg Glu Gln Ser Pro Arg Arg Lys Glu Val Glu Ser Arg Leu Ser
 210 215 220

Pro Gly Glu Ser Ala Tyr Gln Lys Leu Gly Leu Thr Glu Ala His Lys
 225 230 235 240

Trp Arg Pro Asp Ser Arg Glu Ser Gln Glu Gln Ser Leu Val Gln Leu
 245 250 255

Glu Ala Thr Glu Trp Arg Leu Arg Ser Gly Glu Glu Arg Gln Asp Tyr
 260 265 270

Ser Glu Glu Cys Gly Arg Lys Glu Glu Trp Pro Val Pro Gly Val Ala
 275 280 285

Pro Lys Glu Thr Ala Glu Leu Ser Glu Thr Leu Thr Arg Glu Ala Gln
 290 295 300

Gly Asn Ser Ser Ala Gly Val Glu Ala Ala Glu Gln Arg Pro Val Glu
 305 310 315 320

Asp Gly Glu Arg Gly Met Lys Pro Thr Glu Gly Trp Lys Trp Thr Leu
 325 330 335

Asn Ser Gly Lys Ala Arg Glu Trp Thr Pro Arg Asp Ile Glu Ala Gln
 340 345 350

Thr Gln Lys Leu Glu Pro Pro Glu Ser Ala Glu Lys Leu Leu Glu Ser
 355 360 365

Pro Gly Val Glu Ala Gly Glu Gly Glu Ala Glu Lys Glu Glu Ala Gly
 370 375 380

Ala Gln Gly Arg Pro Leu Arg Ala Leu Gln Asn Cys Cys Ser Val Pro
 385 390 395 400

Ser Pro Leu Pro Pro Glu Asp Ala Gly Thr Gly Gly Leu Arg Gln Gln
 405 410 415

Glu Glu Glu Ala Val Glu Leu Gln Pro Pro Pro Pro Ala Pro Leu Ser
 420 425 430

Pro Pro Pro Pro Ala Pro Thr Ala Pro Gln Pro Pro Gly Asp Pro Leu
 435 440 445

Met Ser Arg Leu Phe Tyr Gly Val Lys Ala Gly Pro Gly Val Gly Ala
 450 455 460

Pro Arg Arg Ser Gly His Thr Phe Thr Val Asn Pro Arg Arg Ser Val
 465 470 475 480

Protein Complexes associated with APP-processing
 Pro Pro Ala Thr Pro Ala Thr Pro Thr Ser Pro Ala Thr Val Asp Ala
 485 490 495

Ala Val Pro Gly Ala Gly Lys Lys Arg Tyr Pro Thr Ala Glu Glu Ile
 500 505 510

Leu Val Leu Gly Gly Tyr Leu Arg Leu Ser Arg Ser Cys Leu Ala Lys
 515 520 525

Gly Ser Pro Glu Arg His His Lys Gln Leu Lys Ile Ser Phe Ser Glu
 530 535 540

Thr Ala Leu Glu Thr Thr Tyr Gln Tyr Pro Ser Glu Ser Ser Val Leu
 545 550 555 560

Glu Glu Leu Gly Pro Glu Pro Glu Val Pro Ser Ala Pro Asn Pro Pro
 565 570 575

Ala Ala Gln Pro Asp Asp Glu Glu Asp Glu Glu Glu Leu Leu Leu Leu
 580 585 590

Gln Pro Glu Leu Gln Gly Gly Leu Arg Thr Lys Ala Leu Ile Val Asp
 595 600 605

Glu Ser Cys Arg Arg
 610

<210> 236

<211> 529

<212> PRT

<213> Homo sapiens

<400> 236

Met Ser Glu His Val Glu Pro Ala Ala Pro Gly Pro Gly Pro Asn Gly
 1 5 10 15

Gly Gly Gly Gly Pro Ala Pro Ala Arg Gly Pro Arg Thr Pro Asn Leu
 20 25 30

Asn Pro Asn Pro Leu Ile Asn Val Arg Asp Arg Leu Phe His Ala Leu
 35 40 45

Phe Phe Lys Met Ala Val Thr Tyr Ser Arg Leu Phe Pro Pro Ala Phe
 50 55 60

Arg Arg Leu Phe Glu Phe Phe Val Leu Leu Lys Ala Leu Phe Val Leu
 65 70 75 80

Protein Complexes associated with APP-processing
Phe Val Leu Ala Tyr Ile His Ile Val Phe Ser Arg Ser Pro Ile Asn
85 90 95

Cys Leu Glu His Val Arg Asp Lys Trp Pro Arg Glu Gly Ile Leu Arg
100 105 110

Val Glu Val Arg His Asn Ser Ser Arg Ala Pro Val Phe Leu Gln Phe
115 120 125

Cys Asp Ser Gly Gly Arg Gly Ser Phe Pro Gly Leu Ala Val Glu Pro
130 135 140

Gly Ser Asn Leu Asp Met Glu Asp Glu Glu Glu Glu Glu Leu Thr Met
145 150 155 160

Glu Met Phe Gly Asn Ser Ser Ile Lys Phe Glu Leu Asp Ile Glu Pro
165 170 175

Lys Val Phe Lys Pro Pro Ser Ser Thr Glu Ala Leu Asn Asp Ser Gln
180 185 190

Glu Phe Pro Phe Pro Glu Thr Pro Thr Lys Val Trp Pro Gln Asp Glu
195 200 205

Tyr Ile Val Glu Tyr Ser Leu Glu Tyr Gly Phe Leu Arg Leu Ser Gln
210 215 220

Ala Thr Arg Gln Arg Leu Ser Ile Pro Val Met Val Val Thr Leu Asp
225 230 235 240

Pro Thr Arg Asp Gln Cys Phe Gly Asp Arg Phe Ser Arg Leu Leu Leu
245 250 255

Asp Glu Phe Leu Gly Tyr Asp Asp Ile Leu Met Ser Ser Val Lys Gly
260 265 270

Leu Ala Glu Asn Glu Glu Asn Lys Gly Phe Leu Arg Asn Val Val Ser
275 280 285

Gly Glu His Tyr Arg Phe Val Ser Met Trp Met Ala Arg Thr Ser Tyr
290 295 300

Leu Ala Ala Phe Ala Ile Met Val Ile Phe Thr Leu Ser Val Ser Met
305 310 315 320

Leu Leu Arg Tyr Ser His His Gln Ile Phe Val Phe Ile Val Asp Leu
325 330 335

Leu Gln Met Leu Glu Met Asn Met Ala Ile Ala Phe Pro Ala Ala Pro
340 345 350

Protein Complexes associated with APP-processing
 Leu Leu Thr Val Ile Leu Ala Leu Val Gly Met Glu Ala Ile Met Ser
 355 360 365

Glu Phe Phe Asn Asp Thr Thr Thr Ala Phe Tyr Ile Ile Leu Ile Val
 370 375 380

Trp Leu Ala Asp Gln Tyr Asp Ala Ile Cys Cys His Thr Ser Thr Ser
 385 390 395 400

Lys Arg His Trp Leu Arg Phe Phe Tyr Leu Tyr His Phe Ala Phe Tyr
 405 410 415

Ala Tyr His Tyr Arg Phe Asn Gly Gln Tyr Ser Ser Leu Ala Leu Val
 420 425 430

Thr Ser Trp Leu Phe Ile Gln His Ser Met Ile Tyr Phe Phe His His
 435 440 445

Tyr Glu Leu Pro Ala Ile Leu Gln Gln Val Arg Ile Gln Glu Met Leu
 450 455 460

Leu Gln Ala Pro Pro Leu Gly Pro Gly Thr Pro Thr Ala Leu Pro Asp
 465 470 475 480

Asp Met Asn Asn Asn Ser Gly Ala Pro Ala Thr Ala Pro Asp Ser Ala
 485 490 495

Gly Gln Pro Pro Ala Leu Gly Pro Val Phe Glu Leu Val Ser Lys Glu
 500 505 510

Arg Gly Trp Gly Ser Ala Glu Gly Ser Gly Gly Val Leu Val Gly Leu
 515 520 525

Gln

<210> 237

<211> 378

<212> PRT

<213> Homo sapiens

<400> 237

Lys Glu Gln Ser Glu Leu Asp Gln Asp Leu Asp Asp Val Glu Glu Val
 1 5 10 15

Glu Glu Glu Glu Thr Gly Glu Glu Thr Lys Leu Lys Ala Arg Gln Leu
 20 25 30

Thr Val Gln Met Met Gln Asn Pro Gln Ile Leu Ala Ala Leu Gln Glu
35 40 45

Asp Ser Phe Phe Asn Phe Phe Ala Pro Pro Glu Val Ile Pro Lys Phe
290 295 300

Protein Complexes associated with APP-processing
 Ser Ala Phe Asp Asp Asp Ala Glu Ala Ile Leu Ala Ala Asp Phe Glu
 305 310 315 320

Ile Gly His Phe Leu Arg Glu Arg Ile Ile Pro Arg Ser Val Leu Tyr
 325 330 335

Phe Thr Gly Glu Ala Ile Glu Asp Asp Asp Asp Tyr Asp Glu Glu
 340 345 350

Gly Glu Glu Ala Asp Glu Gly Tyr Gln Leu Phe Glu Glu Val Lys Ser
 355 360 365

Cys Ser Lys Leu Phe Gln Arg Trp Leu Gln
 370 375

<210> 238

<211> 192

<212> PRT

<213> Homo sapiens

<400> 238

Gly Lys Gln Asn Ser Lys Leu Arg Pro Glu Val Met Gln Asp Leu Leu
 1 5 10 15

Glu Ser Thr Asp Phe Thr Glu His Glu Ile Gln Glu Trp Tyr Lys Gly
 20 25 30

Phe Leu Arg Asp Cys Pro Ser Gly His Leu Ser Met Glu Glu Phe Lys
 35 40 45

Lys Ile Tyr Gly Asn Phe Phe Pro Tyr Gly Asp Ala Ser Lys Phe Ala
 50 55 60

Glu His Val Phe Arg Thr Phe Asp Ala Asn Gly Asp Gly Thr Ile Asp
 65 70 75 80

Phe Arg Glu Phe Ile Ile Ala Leu Ser Val Thr Ser Arg Gly Lys Leu
 85 90 95

Glu Gln Lys Leu Lys Trp Ala Phe Ser Met Tyr Asp Leu Asp Gly Asn
 100 105 110

Gly Tyr Ile Ser Lys Ala Glu Met Leu Glu Ile Val Gln Ala Ile Tyr
 115 120 125

Lys Met Val Ser Ser Val Met Lys Met Pro Glu Asp Glu Ser Thr Pro
 130 135 140

Protein Complexes associated with APP-processing
 Glu Lys Arg Thr Glu Lys Ile Phe Arg Gln Met Asp Thr Asn Arg Asp
 145 150 155 160

Gly Lys Leu Ser Leu Glu Glu Phe Ile Arg Gly Ala Lys Ser Asp Pro
 165 170 175

Ser Ile Val Arg Leu Leu Gln Cys Asp Pro Ser Ser Ala Gly Gln Phe
 180 185 190

<210> 239

<211> 482

<212> PRT

<213> Homo sapiens

<400> 239

Met Val Glu Lys Gly Pro Glu Val Ser Gly Lys Arg Arg Gly Arg Asn
 1 5 10 15

Asn Ala Ala Ala Ser Ala Ser Ala Ala Ala Ser Ala Ala Ala Ser
 20 25 30

Ala Ala Cys Ala Ser Pro Ala Ala Thr Ala Ala Ser Gly Ala Ala Ala
 35 40 45

Ser Ser Ala Ser Ala Ala Ala Ala Ser Ala Ala Ala Ala Pro Asn Asn
 50 55 60

Gly Gln Asn Lys Ser Leu Ala Ala Ala Ala Pro Asn Gly Asn Ser Ser
 65 70 75 80

Ser Asn Ser Trp Glu Glu Gly Ser Ser Gly Ser Ser Ser Asp Glu Glu
 85 90 95

His Gly Gly Gly Gly Met Arg Val Gly Pro Gln Tyr Gln Ala Val Val
 100 105 110

Pro Asp Phe Asp Pro Ala Lys Leu Ala Arg Arg Ser Gln Glu Arg Asp
 115 120 125

Asn Leu Gly Met Leu Val Trp Ser Pro Asn Gln Asn Leu Ser Glu Ala
 130 135 140

Lys Leu Asp Glu Tyr Ile Ala Ile Ala Lys Glu Lys His Gly Tyr Asn
 145 150 155 160

Met Glu Gln Ala Leu Gly Met Leu Phe Trp His Lys His Asn Ile Glu
 165 170 175

Protein Complexes associated with APP-processing

Lys Ser Leu Ala Asp Leu Pro Asn Phe Thr Pro Phe Pro Asp Glu Trp
180 185 190

Thr Val Glu Asp Lys Val Leu Phe Glu Gln Ala Phe Ser Phe His Gly
195 200 205

Lys Thr Phe His Arg Ile Gln Gln Met Leu Pro Asp Lys Ser Ile Ala
210 220

Ser Leu Val Lys Phe Tyr Tyr Ser Trp Lys Lys Thr Arg Thr Lys Thr
225 230 235 240

Ser Val Met Asp Arg His Ala Arg Lys Gln Lys Arg Glu Arg Glu Glu
245 250 255

Ser Glu Asp Glu Leu Glu Glu Ala Asn Gly Asn Asn Pro Ile Asp Ile
260 265 270

Glu Val Asp Gln Asn Lys Glu Ser Lys Lys Glu Val Pro Pro Thr Glu
275 280 285

Thr Val Pro Gln Val Lys Lys Glu Lys His Ser Thr Gln Ala Lys Asn
290 295 300

Arg Ala Lys Arg Lys Pro Pro Lys Gly Met Phe Leu Ser Gln Glu Asp
305 310 315 320

Val Glu Ala Val Ser Ala Asn Ala Thr Ala Ala Thr Thr Val Leu Arg
325 330 335

Gln Leu Asp Met Glu Leu Val Ser Val Lys Arg Gln Ile Gln Asn Ile
340 345 350

Lys Gln Thr Asn Ser Ala Leu Lys Glu Lys Leu Asp Gly Gly Ile Glu
355 360 365

Pro Tyr Arg Leu Pro Glu Val Ile Gln Lys Cys Asn Ala Arg Trp Thr
370 375 380

Thr Glu Glu Gln Leu Leu Ala Val Gln Ala Ile Arg Lys Tyr Gly Arg
385 390 395 400

Asp Phe Gln Ala Ile Ser Asp Val Ile Gly Asn Lys Ser Val Val Gln
405 410 415

Val Lys Asn Phe Phe Val Asn Tyr Arg Arg Arg Phe Asn Ile Asp Glu
420 425 430

Val Leu Gln Glu Trp Glu Ala Glu His Gly Lys Glu Glu Thr Asn Gly
435 440 445

Protein Complexes associated with APP-processing
 Pro Ser Asn Gln Lys Pro Val Lys Ser Pro Asp Asn Ser Ile Lys Met
 450 455 460

Pro Glu Glu Glu Asp Glu Ala Pro Val Leu Asp Val Arg Tyr Ala Ser
 465 470 475 480

Ala Ser

<210> 240

<211> 375

<212> PRT

<213> Homo sapiens

<400> 240

Met Asp Asp Asp Ile Ala Ala Leu Val Val Asp Asn Gly Ser Gly Met
 1 5 10 15

Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe Pro
 20 25 30

Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly Met Gly
 35 40 45

Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg Gly Ile
 50 55 60

Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Val Thr Asn Trp Asp
 65 70 75 80

Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu Arg Val
 85 90 95

Ala Pro Glu Glu His Pro Val Leu Leu Thr Glu Ala Pro Leu Asn Pro
 100 105 110

Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe Asn
 115 120 125

Thr Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu Tyr Ala
 130 135 140

Ser Gly Arg Thr Thr Gly Ile Val Met Asp Ser Gly Asp Gly Val Thr
 145 150 155 160

His Thr Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala Ile Leu
 165 170 175

Protein Complexes associated with APP-processing

Protein Complexes associated with APP-processing

Gly Asn Ala Cys Trp Glu Leu Tyr Cys Leu Glu His Gly Ile Gln Pro
 20 25 30

Asp Gly Gln Met Pro Ser Asp Lys Thr Ile Gly Gly Gly Asp Asp Ser
 35 40 45

Phe Asn Thr Phe Phe Ser Glu Thr Gly Ala Gly Lys His Val Pro Arg
 50 55 60

Ala Val Phe Val Asp Leu Glu Pro Thr Val Ile Asp Glu Val Arg Thr
 65 70 75 80

Gly Thr Tyr Arg Gln Leu Phe His Pro Glu Gln Leu Ile Thr Gly Lys
 85 90 95

Glu Asp Ala Ala Asn Asn Tyr Ala Arg Gly His Tyr Thr Ile Gly Lys
 100 105 110

Glu Ile Ile Asp Leu Val Leu Asp Arg Ile Arg Lys Leu Ala Asp Gln
 115 120 125

Cys Thr Gly Leu Gln Gly Phe Leu Val Phe His Ser Phe Gly Gly Gly
 130 135 140

Thr Gly Ser Gly Phe Thr Ser Leu Leu Met Glu Arg Leu Ser Val Asp
 145 150 155 160

Tyr Gly Lys Lys Ser Lys Leu Glu Phe Ser Ile Tyr Pro Ala Pro Gln
 165 170 175

Val Ser Thr Ala Val Val Glu Pro Tyr Asn Ser Ile Leu Thr Thr His
 180 185 190

Thr Thr Leu Glu His Ser Asp Cys Ala Phe Met Val Asp Asn Glu Ala
 195 200 205

Ile Tyr Asp Ile Cys Arg Arg Asn Leu Asp Ile Glu Arg Pro Thr Tyr
 210 215 220

Thr Asn Leu Asn Arg Leu Ile Ser Gln Ile Val Ser Ser Ile Thr Ala
 225 230 235 240

Ser Leu Arg Phe Asp Gly Ala Leu Asn Val Asp Leu Thr Glu Phe Gln
 245 250 255

Thr Asn Leu Val Pro Tyr Pro Arg Ile His Phe Pro Leu Ala Thr Tyr
 260 265 270

Ala Pro Val Ile Ser Ala Glu Lys Ala Tyr His Glu Gln Leu Ser Val
 275 280 285

Protein Complexes associated with APP-processing
 Ala Glu Ile Thr Asn Ala Cys Phe Glu Pro Ala Asn Gln Met Val Lys
 290 295 300

Cys Asp Pro Arg His Gly Lys Tyr Met Ala Cys Cys Leu Leu Tyr Arg
 305 310 315 320

Gly Asp Val Val Pro Lys Asp Val Asn Ala Ala Ile Ala Thr Ile Lys
 325 330 335

Thr Lys Arg Ser Ile Gln Phe Val Asp Trp Cys Pro Thr Gly Phe Lys
 340 345 350

Val Gly Ile Asn Tyr Gln Pro Pro Thr Val Val Pro Gly Gly Asp Leu
 355 360 365

Ala Lys Val Gln Arg Ala Val Cys Met Leu Ser Asn Thr Thr Ala Ile
 370 375 380

Ala Glu Ala Trp Ala Arg Leu Asp His Lys Phe Asp Leu Met Tyr Ala
 385 390 395 400

Lys Arg Ala Phe Val His Trp Tyr Val Gly Glu Gly Met Glu Glu Gly
 405 410 415

Glu Phe Ser Glu Ala Arg Glu Asp Met Ala Ala Leu Glu Lys Asp Tyr
 420 425 430

Glu Glu Val Gly Val Asp Ser Val Glu Gly Glu Gly Glu Glu Glu Gly
 435 440 445

Glu Glu Tyr
 450

<210> 242

<211> 444

<212> PRT

<213> Homo sapiens

<400> 242

Met Arg Glu Ile Val His Ile Gln Ala Gly Gln Cys Gly Asn Gln Ile
 1 5 10 15

Gly Ala Lys Phe Trp Glu Val Ile Ser Asp Glu His Gly Ile Asp Pro
 20 25 30

Thr Gly Thr Tyr His Gly Asp Ser Asp Leu Gln Leu Asp Arg Ile Ser
 35 40 45

Protein Complexes associated with APP-processing

Val Tyr Tyr Asn Glu Ala Thr Gly Gly Lys Tyr Val Pro Arg Ala Ile
50 55 60

Leu Val Asp Leu Glu Pro Gly Thr Met Asp Ser Val Arg Ser Gly Pro
65 70 75 80

Phe Gly Gln Ile Phe Arg Pro Asp Asn Phe Val Phe Gly Gln Ser Gly
85 90 95

Ala Gly Asn Asn Trp Ala Lys Gly His Tyr Thr Glu Gly Ala Glu Leu
100 105 110

Val Asp Ser Val Leu Asp Val Val Arg Lys Glu Ala Glu Ser Cys Asp
115 120 125

Cys Leu Gln Gly Phe Gln Leu Thr His Ser Leu Gly Gly Gly Thr Gly
130 135 140

Ser Gly Met Gly Thr Leu Leu Ile Ser Lys Ile Arg Glu Glu Tyr Pro
145 150 155 160

Asp Arg Ile Met Asn Thr Phe Ser Val Val Pro Ser Pro Lys Val Ser
165 170 175

Asp Thr Val Val Glu Pro Tyr Asn Ala Thr Leu Ser Val His Gln Leu
180 185 190

Val Glu Asn Thr Asp Glu Thr Tyr Cys Ile Asp Asn Glu Ala Leu Tyr
195 200 205

Asp Ile Cys Phe Arg Thr Leu Lys Leu Thr Thr Pro Thr Tyr Gly Asp
210 215 220

Leu Asn His Leu Val Ser Ala Thr Met Ser Gly Val Thr Thr Cys Leu
225 230 235 240

Arg Phe Pro Gly Gln Leu Asn Ala Asp Leu Arg Lys Leu Ala Val Asn
245 250 255

Met Val Pro Phe Pro Arg Leu His Phe Phe Met Pro Gly Phe Ala Pro
260 265 270

Leu Thr Ser Arg Gly Ser Gln Gln Tyr Arg Ala Leu Thr Val Pro Glu
275 280 285

Leu Thr Gln Gln Val Phe Asp Ala Lys Asn Met Met Ala Ala Cys Asp
290 295 300

Pro Arg His Gly Arg Tyr Leu Thr Val Ala Ala Val Phe Arg Gly Arg
305 310 315 320

Protein Complexes associated with APP-processing

Met	Ser	Met	Lys	Glu	Val	Asp	Glu	Gln	Met	Leu	Asn	Val	Gln	Asn	Lys
				325					330					335	

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Protein Complexes associated with APP-processing

Cys Thr Ile Phe Leu Gly Tyr Thr Ser Asn Leu Ile Ser Ser Gly Ile
100 105 110

Arg Glu Thr Ile Arg Tyr Leu Val Gln His Asn Met Val Asp Val Leu
115 120 125

Val Thr Thr Ala Gly Gly Val Glu Glu Asp Leu Ile Lys Cys Leu Ala
130 135 140

Pro Thr Tyr Leu Gly Glu Phe Ser Leu Arg Gly Lys Glu Leu Arg Glu
145 150 155 160

Asn Gly Ile Asn Arg Ile Gly Asn Leu Leu Val Pro Asn Glu Asn Tyr
165 170 175

Cys Lys Phe Glu Asp Trp Leu Met Pro Ile Leu Asp Gln Met Val Met
180 185 190

Glu Gln Asn Thr Glu Gly Val Lys Trp Thr Pro Ser Lys Met Ile Ala
195 200 205

Arg Leu Gly Lys Glu Ile Asn Asn Pro Glu Ser Val Tyr Tyr Trp Ala
210 215 220

Gln Lys Asn His Ile Pro Val Phe Ser Pro Ala Leu Thr Asp Gly Ser
225 230 235 240

Leu Gly Asp Met Ile Phe Phe His Ser Tyr Lys Asn Pro Gly Leu Val
245 250 255

Leu Asp Ile Val Glu Asp Leu Arg Leu Ile Asn Thr Gln Ala Ile Phe
260 265 270

Ala Lys Cys Thr Gly Met Ile Ile Leu Gly Gly Gly Val Val Lys His
275 280 285

His Ile Ala Asn Ala Asn Leu Met Arg Asn Gly Ala Asp Tyr Ala Val
290 295 300

Tyr Ile Asn Thr Ala Gln Glu Phe Asp Gly Ser Asp Ser Gly Ala Arg
305 310 315 320

Pro Asp Glu Ala Val Ser Trp Gly Lys Ile Arg Val Asp Ala Gln Pro
325 330 335

Val Lys Val Tyr Ala Asp Ala Ser Leu Val Phe Pro Leu Leu Val Ala
340 345 350

Glu Thr Phe Ala Gln Lys Met Asp Ala Phe Met His Glu Lys Asn Glu
355 360 365

Protein Complexes associated with APP-processing

Asp

<210> 244

<211> 401

<212> PRT

<213> Homo sapiens

<400> 244

Met Ala Asp Pro Lys Tyr Ala Asp Leu Pro Gly Ile Ala Arg Asn Glu
 1 5 10 15

Pro Asp Val Tyr Glu Thr Ser Asp Leu Pro Glu Asp Asp Gln Ala Glu
 20 25 30

Phe Asp Ala Glu Glu Leu Thr Ser Thr Ser Val Glu His Ile Ile Val
 35 40 45

Asn Pro Asn Ala Ala Tyr Asp Lys Phe Lys Asp Lys Arg Val Gly Thr
 50 55 60

Lys Gly Leu Asp Phe Ser Asp Arg Ile Gly Lys Thr Lys Arg Thr Gly
 65 70 75 80

Tyr Glu Ser Gly Glu Tyr Glu Met Leu Gly Glu Gly Leu Gly Val Lys
 85 90 95

Glu Thr Pro Gln Gln Lys Tyr Gln Arg Leu Leu His Glu Val Gln Glu
 100 105 110

Leu Thr Thr Glu Val Glu Lys Ile Lys Thr Thr Val Lys Glu Ser Ala
 115 120 125

Thr Glu Glu Lys Leu Thr Pro Val Leu Leu Ala Lys Gln Leu Ala Ala
 130 135 140

Leu Lys Gln Gln Leu Val Ala Ser His Leu Glu Lys Leu Leu Gly Pro
 145 150 155 160

Asp Ala Ala Ile Asn Leu Thr Asp Pro Asp Gly Ala Leu Ala Lys Arg
 165 170 175

Leu Leu Leu Gln Leu Glu Ala Thr Lys Asn Ser Lys Gly Gly Ser Gly
 180 185 190

Gly Lys Thr Thr Gly Thr Pro Pro Asp Ser Ser Leu Val Thr Tyr Glu
 195 200 205

Protein Complexes associated with APP-processing
 Leu His Ser Arg Pro Glu Gln Asp Lys Phe Ser Gln Ala Ala Lys Val
 210 215 220

Ala Glu Leu Glu Lys Arg Leu Thr Glu Leu Glu Thr Ala Val Arg Cys
 225 230 235 240

Asp Gln Asp Ala Gln Asn Pro Leu Ser Ala Gly Leu Gln Gly Ala Cys
 245 250 255

Leu Met Glu Thr Val Glu Leu Leu Gln Ala Lys Val Ser Ala Leu Asp
 260 265 270

Leu Ala Val Leu Asp Gln Val Glu Ala Arg Leu Gln Ser Val Leu Gly
 275 280 285

Lys Val Asn Glu Ile Ala Lys His Lys Ala Ser Val Glu Asp Ala Asp
 290 295 300

Thr Gln Ser Lys Val His Gln Leu Tyr Glu Thr Ile Gln Arg Trp Ser
 305 310 315 320

Pro Ile Ala Ser Thr Leu Pro Glu Leu Val Gln Arg Leu Val Thr Ile
 325 330 335

Lys Gln Leu His Glu Gln Ala Met Gln Phe Gly Gln Leu Leu Thr His
 340 345 350

Leu Asp Thr Thr Gln Gln Met Ile Ala Asn Ser Leu Lys Asp Asn Thr
 355 360 365

Thr Leu Leu Thr Gln Val Gln Thr Thr Met Arg Glu Asn Leu Ala Thr
 370 375 380

Val Glu Gly Asn Phe Ala Ser Ile Asp Glu Arg Met Lys Lys Leu Gly
 385 390 395 400

Lys

<210> 245

<211> 342

<212> PRT

<213> Homo sapiens

<400> 245

Met Arg Lys Glu Thr Pro Pro Pro Leu Val Pro Pro Ala Ala Arg Glu
 1 5 10 15

Protein Complexes associated with APP-processing

Ser Leu Ser Glu Asp Cys Ser Leu Ala Val Leu Asp Ser Ser Leu Ser
275 280 285

Protein Complexes associated with APP-processing

Glu Leu Phe Arg Ser Gln Ala His Arg Asp Phe Val Arg Asp Ala Thr
 290 295 300

Trp Ser Pro Leu Asn His Ser Leu Leu Thr Thr Val Gly Trp Asp His
 305 310 315 320

Gln Val Val His His Val Val Pro Thr Glu Pro Leu Pro Ala Pro Gly
 325 330 335

Pro Ala Ser Val Thr Glu
 340

<210> 246

<211> 514

<212> PRT

<213> Homo sapiens

<400> 246

Met Ser Ile Ser Ser Asp Glu Val Asn Phe Leu Val Tyr Arg Tyr Leu
 1 5 10 15

Gln Glu Ser Gly Phe Ser His Ser Ala Phe Thr Phe Gly Ile Glu Ser
 20 25 30

His Ile Ser Gln Ser Asn Ile Asn Gly Ala Leu Val Pro Pro Ala Ala
 35 40 45

Leu Ile Ser Ile Ile Gln Lys Gly Leu Gln Tyr Val Glu Ala Glu Val
 50 55 60

Ser Ile Asn Glu Asp Gly Thr Leu Phe Asp Gly Arg Pro Ile Glu Ser
 65 70 75 80

Leu Ser Leu Ile Asp Ala Val Met Pro Asp Val Val Gln Thr Arg Gln
 85 90 95

Gln Ala Tyr Arg Asp Lys Leu Ala Gln Gln Gln Ala Ala Ala Ala Ala
 100 105 110

Ala Ala Ala Ala Ala Ala Ser Gln Gln Gly Ser Ala Lys Asn Gly Glu
 115 120 125

Asn Thr Ala Asn Gly Glu Glu Asn Gly Ala His Thr Ile Ala Asn Asn
 130 135 140

His Thr Asp Met Met Glu Val Asp Gly Asp Val Glu Ile Pro Pro Asn
 145 150 155 160

Protein Complexes associated with APP-processing

Lys Ala Val Val Leu Arg Gly His Glu Ser Glu Val Phe Ile Cys Ala
165 170 175

Trp Asn Pro Val Ser Asp Leu Leu Ala Ser Gly Ser Gly Asp Ser Thr
180 185 190

Ala Arg Ile Trp Asn Leu Ser Glu Asn Ser Thr Ser Gly Ser Thr Gln
195 200 205

Leu Val Leu Arg His Cys Ile Arg Glu Gly Gly Gln Asp Val Pro Ser
210 215 220

Asn Lys Asp Val Thr Ser Leu Asp Trp Asn Ser Glu Gly Thr Leu Leu
225 230 235 240

Ala Thr Gly Ser Tyr Asp Gly Phe Ala Arg Ile Trp Thr Lys Asp Gly
245 250 255

Asn Leu Ala Ser Thr Leu Gly Gln His Lys Gly Pro Ile Phe Ala Leu
260 265 270

Lys Trp Asn Lys Lys Gly Asn Phe Ile Leu Ser Ala Gly Val Asp Lys
275 280 285

Thr Thr Ile Ile Trp Asp Ala His Thr Gly Glu Ala Lys Gln Gln Phe
290 295 300

Pro Phe His Ser Ala Pro Ala Leu Asp Val Asp Trp Gln Ser Asn Asn
305 310 315 320

Thr Phe Ala Ser Cys Ser Thr Asp Met Cys Ile His Val Cys Lys Leu
325 330 335

Gly Gln Asp Arg Pro Ile Lys Thr Phe Gln Gly His Thr Asn Glu Val
340 345 350

Asn Ala Ile Lys Trp Asp Pro Thr Gly Asn Leu Leu Ala Ser Cys Ser
355 360 365

Asp Asp Met Thr Leu Lys Ile Trp Ser Met Lys Gln Asp Asn Cys Val
370 375 380

His Asp Leu Gln Ala His Asn Lys Glu Ile Tyr Thr Ile Lys Trp Ser
385 390 395 400

Pro Thr Gly Pro Gly Thr Asn Asn Pro Asn Ala Asn Leu Met Leu Ala
405 410 415

Ser Ala Ser Phe Asp Ser Thr Val Arg Leu Trp Asp Val Asp Arg Gly
420 425 430

Protein Complexes associated with APP-processing

Ile Cys Ile His Thr Leu Thr Lys His Gln Glu Pro Val Tyr Ser Val
 435 440 445

Ala Phe Ser Pro Asp Gly Arg Tyr Leu Ala Ser Gly Ser Phe Asp Lys
 450 455 460

Cys Val His Ile Trp Asn Thr Gln Thr Gly Ala Leu Val His Ser Tyr
 465 470 475 480

Arg Gly Thr Gly Gly Ile Phe Glu Val Cys Trp Asn Ala Ala Gly Asp
 485 490 495

Lys Val Gly Ala Ser Ala Ser Asp Gly Ser Val Cys Val Leu Asp Leu
 500 505 510

Arg Lys

<210> 247

<211> 309

<212> PRT

<213> Homo sapiens

<400> 247

Met Asp Glu Lys Val Phe Thr Lys Glu Leu Asp Gln Trp Ile Glu Gln
 1 5 10 15

Leu Asn Glu Cys Lys Gln Leu Ser Glu Ser Gln Val Lys Ser Leu Cys
 20 25 30

Glu Lys Ala Lys Glu Ile Leu Thr Lys Glu Ser Asn Val Gln Glu Val
 35 40 45

Arg Cys Pro Val Thr Val Cys Gly Asp Val His Gly Gln Phe His Asp
 50 55 60

Leu Met Glu Leu Phe Arg Ile Gly Gly Lys Ser Pro Asp Thr Asn Tyr
 65 70 75 80

Leu Phe Met Gly Asp Tyr Val Asp Arg Gly Tyr Tyr Ser Val Glu Thr
 85 90 95

Val Thr Leu Leu Val Ala Leu Lys Val Arg Tyr Arg Glu Arg Ile Thr
 100 105 110

Ile Leu Arg Gly Asn His Glu Ser Arg Gln Ile Thr Gln Val Tyr Gly
 115 120 125

Protein Complexes associated with APP-processing
 Phe Tyr Asp Glu Cys Leu Arg Lys Tyr Gly Asn Ala Asn Val Trp Lys
 130 135 140

Tyr Phe Thr Asp Leu Phe Asp Tyr Leu Pro Leu Thr Ala Leu Val Asp
 145 150 155 160

Gly Gln Ile Phe Cys Leu His Gly Gly Leu Ser Pro Ser Ile Asp Thr
 165 170 175

Leu Asp His Ile Arg Ala Leu Asp Arg Leu Gln Glu Val Pro His Glu
 180 185 190

Gly Pro Met Cys Asp Leu Leu Trp Ser Asp Pro Asp Asp Arg Gly Gly
 195 200 205

Trp Gly Ile Ser Pro Arg Gly Ala Gly Tyr Thr Phe Gly Gln Asp Ile
 210 215 220

Ser Glu Thr Phe Asn His Ala Asn Gly Leu Thr Leu Val Ser Arg Ala
 225 230 235 240

His Gln Leu Val Met Glu Gly Tyr Asn Trp Cys His Asp Arg Asn Val
 245 250 255

Val Thr Ile Phe Ser Ala Pro Asn Tyr Cys Tyr Arg Cys Gly Asn Gln
 260 265 270

Ala Ala Ile Met Glu Leu Asp Asp Thr Leu Lys Tyr Ser Phe Leu Gln
 275 280 285

Phe Asp Pro Ala Pro Arg Arg Gly Glu Pro His Val Thr Arg Arg Thr
 290 295 300

Pro Asp Tyr Phe Leu
 305

<210> 248

<211> 309

<212> PRT

<213> Homo sapiens

<400> 248

Met Asp Asp Lys Ala Phe Thr Lys Glu Leu Asp Gln Trp Val Glu Gln
 1 5 10 15

Leu Asn Glu Cys Lys Gln Leu Asn Glu Asn Gln Val Arg Thr Leu Cys
 20 25 30

protein Complexes associated with APP-processing

Glu Lys Ala Lys Glu Ile Leu Thr Lys Glu Ser Asn Val Gln Glu Val
 35 40 45

Arg Cys Pro Val Thr Val Cys Gly Asp Val His Gly Gln Phe His Asp
 50 55 60

Leu Met Glu Leu Phe Arg Ile Gly Gly Lys Ser Pro Asp Thr Asn Tyr
 65 70 75 80

Leu Phe Met Gly Asp Tyr Val Asp Arg Gly Tyr Tyr Ser Val Glu Thr
 85 90 95

Val Thr Leu Leu Val Ala Leu Lys Val Arg Tyr Pro Glu Arg Ile Thr
 100 105 110

Ile Leu Arg Gly Asn His Glu Ser Arg Gln Ile Thr Gln Val Tyr Gly
 115 120 125

Phe Tyr Asp Glu Cys Leu Arg Lys Tyr Gly Asn Ala Asn Val Trp Lys
 130 135 140

Tyr Phe Thr Asp Leu Phe Asp Tyr Leu Pro Leu Thr Ala Leu Val Asp
 145 150 155 160

Gly Gln Ile Phe Cys Leu His Gly Gly Leu Ser Pro Ser Ile Asp Thr
 165 170 175

Leu Asp His Ile Arg Ala Leu Asp Arg Leu Gln Glu Val Pro His Glu
 180 185 190

Gly Pro Met Cys Asp Leu Leu Trp Ser Asp Pro Asp Asp Arg Gly Gly
 195 200 205

Trp Gly Ile Ser Pro Arg Gly Ala Gly Tyr Thr Phe Gly Gln Asp Ile
 210 215 220

Ser Glu Thr Phe Asn His Ala Asn Gly Leu Thr Leu Val Ser Arg Ala
 225 230 235 240

His Gln Leu Val Met Glu Gly Tyr Asn Trp Cys His Asp Arg Asn Val
 245 250 255

Val Thr Ile Phe Ser Ala Pro Asn Tyr Cys Tyr Arg Cys Gly Asn Gln
 260 265 270

Ala Ala Ile Met Glu Leu Asp Asp Thr Leu Lys Tyr Ser Phe Leu Gln
 275 280 285

Phe Asp Pro Ala Pro Arg Arg Gly Glu Pro His Val Thr Arg Arg Thr
 290 295 300

Protein Complexes associated with APP-processing

Pro Asp Tyr Phe Leu
305

<210> 249

<211> 588

<212> PRT

<213> Homo sapiens

<400> 249

Ala Ala Ala Asp Gly Asp Asp Ser Leu Tyr Pro Ile Ala Val Leu Ile
1 5 10 15Asp Glu Leu Arg Asn Glu Asp Val Gln Leu Arg Leu Asn Ser Ile Lys
20 25 30Lys Leu Ser Thr Ile Ala Leu Ala Leu Gly Val Glu Arg Thr Arg Ser
35 40 45Glu Leu Leu Pro Phe Leu Thr Asp Thr Ile Tyr Asp Glu Asp Glu Val
50 55 60Leu Leu Ala Leu Ala Glu Gln Leu Gly Thr Phe Thr Thr Leu Val Gly
65 70 75 80Gly Pro Glu Tyr Val His Cys Leu Leu Pro Pro Leu Glu Ser Leu Ala
85 90 95Thr Val Glu Glu Thr Val Val Arg Asp Lys Ala Val Glu Ser Leu Arg
100 105 110Ala Ile Ser His Glu His Ser Pro Ser Asp Leu Glu Ala His Phe Val
115 120 125Pro Leu Val Lys Arg Leu Ala Gly Gly Asp Trp Phe Thr Ser Arg Thr
130 135 140Ser Ala Cys Gly Leu Phe Ser Val Cys Tyr Pro Arg Val Ser Ser Ala
145 150 155 160Val Lys Ala Glu Leu Arg Gln Tyr Phe Arg Asn Leu Cys Ser Asp Asp
165 170 175Thr Pro Met Val Arg Arg Ala Ala Ala Ser Lys Leu Gly Glu Phe Ala
180 185 190Lys Val Leu Glu Leu Asp Asn Val Lys Ser Glu Ile Ile Pro Met Phe
195 200 205

Protein Complexes associated with APP-processing
 Ser Asn Leu Ala Ser Asp Glu Gln Asp Ser Val Arg Leu Leu Ala Val
 210 215 220

Glu Ala Cys Val Asn Ile Ala Gln Leu Leu Pro Gln Glu Asp Leu Glu
 225 230 235 240

Ala Leu Val Met Pro Thr Leu Arg Gln Ala Ala Glu Asp Lys Ser Trp
 245 250 255

Ala Val Arg Tyr Met Val Ala Asp Lys Phe Thr Glu Leu Gln Lys Ala
 260 265 270

Val Gly Pro Glu Ile Thr Lys Thr Asp Leu Val Pro Ala Phe Gln Asn
 275 280 285

Leu Met Lys Asp Cys Glu Ala Glu Val Arg Ala Ala Ala Ser His Lys
 290 295 300

Val Lys Glu Phe Cys Glu Asn Leu Ser Ala Asp Cys Arg Glu Asn Val
 305 310 315 320

Ile Met Ser Gln Ile Leu Pro Cys Ile Lys Glu Leu Val Ser Asp Ala
 325 330 335

Asn Gln His Val Lys Ser Ala Leu Ala Ser Val Ile Met Gly Leu Ser
 340 345 350

Pro Ile Leu Gly Lys Asp Asn Thr Ile Glu His Leu Leu Pro Leu Phe
 355 360 365

Leu Ala Gln Leu Lys Asp Glu Cys Pro Glu Val Arg Leu Asn Ile Ile
 370 375 380

Ser Asn Leu Asp Cys Val Asn Glu Val Ile Gly Ile Arg Gln Leu Ser
 385 390 395 400

Gln Ser Leu Leu Pro Ala Ile Val Glu Leu Ala Glu Asp Ala Lys Trp
 405 410 415

Arg Val Arg Leu Ala Ile Ile Glu Tyr Met Pro Leu Leu Ala Gly Gln
 420 425 430

Leu Gly Val Glu Phe Phe Asp Glu Lys Leu Asn Ser Leu Cys Met Ala
 435 440 445

Trp Leu Val Asp His Val Tyr Ala Ile Arg Glu Ala Ala Thr Ser Asn
 450 455 460

Leu Lys Lys Leu Val Glu Lys Phe Gly Lys Glu Trp Ala His Ala Thr
 465 470 475 480

Ile Ile Pro Lys Val Leu Ala Met Ser Gly Asp Pro Asn Tyr Leu His
485 490 495

Arg Met Thr Thr Leu Phe Cys Ile Asn Val Leu Ser Glu Val Cys Gly
500 505 510

Gln Asp Ile Thr Thr Lys His Met Leu Pro Thr Val Leu Arg Met Ala
515 520 525

Gly Asp Pro Val Ala Asn Val Arg Phe Asn Val Ala Lys Ser Leu Gln
530 535 540

Lys Ile Gly Pro Ile Leu Asp Asn Ser Thr Leu Gln ser Glu Val Lys
545 550 555 560

Pro Ile Leu Glu Lys Leu Thr Gln Asp Gln Asp Val Asp Val Lys Tyr
565 570 575

Phe Ala Gln Glu Ala Leu Thr Val Leu Ser Leu Ala
580 585

<210> 250

<211> 441

<212> PRT

<213> Homo sapiens

<400> 250

Met Ala Glu Pro Arg Gln Glu Phe Glu Val Met Glu Asp His Ala Gly
1 5 10 15

Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly Tyr Thr Met His
20 25 30

Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Glu Ser Pro Leu
35 40 45

Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr Ser
50 55 60

Asp Ala Lys Ser Thr Pro Thr Ala Glu Asp Val Thr Ala Pro Leu Val
65 . 70 75 80

Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln Pro His Thr Glu
85 90 95

Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile Gly Asp Thr Pro
100 105 110

Protein Complexes associated with APP-processing
 Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln Ala Arg Met Val
 115 120 125

Ser Lys Ser Lys Asp Gly Thr Gly Ser Asp Asp Lys Lys Ala Lys Gly
 130 135 140

Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly Ala Ala Pro Pro
 145 150 155 160

Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro Ala Lys Thr Pro
 165 170 175

Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro Pro Lys Ser Gly
 180 185 190

Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly Thr Pro Gly Ser
 195 200 205

Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr Arg Glu Pro Lys
 210 215 220

Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro Ser Ser Ala Lys
 225 230 235 240

Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn Val
 245 250 255

Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly Gly
 260 265 270

Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val Gln
 275 280 285

Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly Gly
 290 295 300

Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr Ser
 305 310 315 320

Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly Gln
 325 330 335

Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln Ser
 340 345 350

Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly Asn
 355 360 365

Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu Asn Ala Lys Ala
 370 375 380

Protein Complexes associated with APP-processing
 Lys Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser Pro Val Val Ser
 385 390 395 400

Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser Ser Thr Gly Ser
 405 410 415

Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu Ala Asp Glu Val
 420 425 430

Ser Ala Ser Leu Ala Lys Gln Gly Leu
 435 440

<210> 251

<211> 179

<212> PRT

<213> Homo sapiens

<400> 251

Gly Leu Thr Ile Ser Ser Leu Phe Ser Arg Leu Phe Gly Lys Lys Gln
 1 5 10 15

Met Arg Ile Leu Met Val Gly Leu Asp Ala Ala Gly Lys Thr Thr Ile
 20 25 30

Leu Tyr Lys Leu Lys Leu Gly Glu Ile Val Thr Thr Ile Pro Thr Ile
 35 40 45

Gly Phe Asn Val Glu Thr Val Glu Tyr Lys Asn Ile Cys Phe Thr Val
 50 55 60

Trp Asp Val Gly Gly Gln Asp Arg Ile Arg Pro Leu Trp Lys His Tyr
 65 70 75 80

Phe Gln Asn Thr Gln Gly Leu Ile Phe Val Val Asp Ser Asn Asp Arg
 85 90 95

Glu Arg Ile Gln Glu Val Ala Asp Glu Leu Gln Lys Met Leu Leu Val
 100 105 110

Asp Glu Leu Arg Asp Ala Val Leu Leu Leu Phe Ala Asn Lys Gln Asp
 115 120 125

Leu Pro Asn Ala Met Ala Ile Ser Glu Met Thr Asp Lys Leu Gly Leu
 130 135 140

Gln Ser Leu Arg Asn Arg Thr Trp Tyr Val Gln Ala Thr Cys Ala Thr
 145 150 155 160

Protein Complexes associated with APP-processing
 Gln Gly Thr Gly Leu Tyr Glu Gly Leu Asp Trp Leu Ser Asn Glu Leu
 165 170 175

Ser Lys Arg

<210> 252

<211> 564

<212> PRT

<213> Homo sapiens

<400> 252

Glu Asp Ser Leu Leu Lys Asp Leu Phe Gln Asp Tyr Glu Arg Trp Val
 1 5 10 15

Arg Pro Val Glu His Leu Asn Asp Lys Ile Lys Ile Lys Phe Gly Leu
 20 25 30

Ala Ile Ser Gln Leu Val Asp Val Asp Glu Lys Asn Gln Leu Met Thr
 35 40 45

Thr Asn Val Trp Leu Lys Gln Glu Trp Ile Asp Val Lys Leu Arg Trp
 50 55 60

Asn Pro Asp Asp Tyr Gly Gly Ile Lys Val Ile Arg Val Pro Ser Asp
 65 70 75 80

Ser Val Trp Thr Pro Asp Ile Val Leu Phe Asp Asn Ala Val Gly Asp
 85 90 95

Phe Gln Val Asp Asp Lys Thr Lys Ala Leu Leu Lys Tyr Thr Gly Glu
 100 105 110

Val Thr Trp Ile Pro Pro Ala Ile Phe Lys Ser Ser Cys Lys Ile Asp
 115 120 125

Val Thr Tyr Phe Pro Phe Asp Tyr Gln Asn Cys Thr Met Lys Phe Gly
 130 135 140

Ser Trp Ser Tyr Asp Lys Ala Lys Ile Asp Leu Val Leu Ile Gly Ser
 145 150 155 160

Ser Met Asn Leu Lys Asp Tyr Trp Glu Ser Gly Glu Trp Ala Ile Ile
 165 170 175

Lys Ala Pro Gly Tyr Lys His Asp Ile Lys Tyr Asn Cys Cys Glu Glu
 180 185 190

Protein Complexes associated with APP-processing

Ile Tyr Pro Asp Ile Thr Tyr Ser Leu Tyr Ile Arg Arg Leu Pro Leu
195 200 205

Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser Phe Leu
210 215 220

Thr Val Leu Val Phe Tyr Leu Pro Ser Asp Cys Gly Glu Lys Val Thr
225 230 235 240

Leu Cys Ile Ser Val Leu Leu Ser Leu Thr Val Phe Leu Leu Val Ile
245 250 255

Thr Glu Thr Ile Pro Ser Thr Ser Leu Val Ile Pro Leu Ile Gly Glu
260 265 270

Tyr Leu Leu Phe Thr Met Ile Phe Val Thr Leu Ser Ile Val Ile Thr
275 280 285

Val phe Val Leu Asn Val His Tyr Arg Thr Pro Thr Thr His Thr Met
290 295 300

Pro Ser Trp Val Lys Thr Val Phe Leu Asn Leu Leu Pro Arg Val Met
305 310 315 320

Phe Met Thr Arg Pro Thr Ser Asn Glu Gly Asn Ala Gln Lys Pro Arg
325 330 335

Pro Leu Tyr Gly Ala Glu Leu Ser Asn Leu Asn Cys Phe Ser Arg Ala
340 345 350

Glu Ser Lys Gly Cys Lys Glu Gly Tyr Pro Cys Gln Asp Gly Ile Ser
355 360 365

Cys His Pro Pro Pro Ser Met Cys Leu Ser Ser Ala Ser Thr Ser Cys
370 375 380

Ser Pro Trp Cys Trp Ser Pro Ser Pro Ser Ser Pro Ala Ser Val Cys
385 390 395 400

Ser Met Cys Thr Thr Ala Arg Pro Ala Pro Thr Pro Trp His Pro Gly
405 410 415

Ser Ser Ala Ala Ser Cys Thr Ser Cys Leu Pro Ser Ser Ser Lys Arg
420 425 430

Pro Gly Pro Asp Ser Ser Pro Ala Arg Ala Phe Pro Pro Ser Lys Ser
435 440 445

Cys Val Thr Lys Pro Glu Ala Thr Ala Thr Ser Thr Ser Pro Ser Asn
450 455 460

Protein Complexes associated with APP-processing

Phe Tyr Gly Asn Ser Met Tyr Phe Val Asn Pro Ala Ser Ala Ala Ser
 465 470 475 480

Lys Ser Pro Ala Gly Ser Thr Pro Val Ala Ile Pro Arg Asp Phe Trp
 485 490 495

Leu Arg Ser Ser Gly Arg Phe Arg Gln Asp Val Gln Glu Ala Leu Glu
 500 505 510

Gly Val Ser Phe Ile Ala Gln His Met Lys Asn Asp Asp Glu Asp Gln
 515 520 525

Ser Val Val Glu Asp Trp Lys Tyr Val Ala Met Val Val Asp Arg Leu
 530 535 540

Phe Leu Trp Val Phe Met Phe Val Cys Val Leu Gly Thr Val Gly Leu
 545 550 555 560

Phe Leu Pro Pro

<210> 253

<211> 362

<212> PRT

<213> Homo sapiens

<400> 253

Met Val Trp Pro Trp Val Ala Met Ala Ser Arg Trp Gly Pro Leu Ile
 1 5 10 15

Gly Leu Ala Pro Cys Cys Leu Trp Leu Leu Gly Ala Val Leu Leu Met
 20 25 30

Asp Ala Ser Ala Arg Pro Ala Asn His Ser Ser Thr Arg Glu Arg Val
 35 40 45

Ala Asn Arg Glu Glu Asn Glu Ile Leu Pro Pro Asp His Leu Asn Gly
 50 55 60

Val Lys Leu Glu Met Asp Gly His Leu Asn Arg Gly Phe His Gln Glu
 65 70 75 80

Val Phe Leu Gly Lys Asp Leu Gly Gly Phe Asp Glu Asp Ala Glu Pro
 85 90 95

Arg Arg Ser Arg Arg Lys Leu Met Val Ile Phe Ser Lys Val Asp Val
 100 105 110

Protein Complexes associated with APP-processing
 Asn Thr Asp Arg Lys Ile Ser Ala Lys Glu Met Gln Arg Trp Ile Met
 115 120 125

Glu Lys Thr Ala Glu His Phe Gln Glu Ala Met Glu Glu Ser Lys Thr
 130 135 140

His Phe Arg Ala Val Asp Pro Asp Gly Asp Gly His Val Ser Trp Asp
 145 150 155 160

Glu Tyr Lys Val Lys Phe Leu Ala Ser Lys Gly His Ser Glu Lys Glu
 165 170 175

Val Ala Asp Ala Ile Arg Leu Asn Glu Glu Leu Lys Val Asp Glu Glu
 180 185 190

Thr Gln Glu Val Leu Glu Asn Leu Lys Asp Arg Trp Tyr Gln Ala Asp
 195 200 205

Ser Pro Pro Ala Asp Leu Leu Leu Thr Glu Glu Glu Phe Leu Ser Phe
 210 215 220

Leu His Pro Glu His Ser Arg Gly Met Leu Arg Phe Met Val Lys Glu
 225 230 235 240

Ile Val Arg Asp Leu Asp Gln Asp Gly Asp Lys Gln Leu Ser Val Pro
 245 250 255

Glu Phe Ile Ser Leu Pro Val Gly Thr Val Glu Asn Gln Gln Gly Gln
 260 265 270

Asp Ile Asp Asp Asn Trp Val Lys Asp Arg Lys Lys Glu Phe Glu Glu
 275 280 285

Leu Ile Asp Ser Asn His Asp Gly Ile Val Thr Ala Glu Glu Leu Glu
 290 295 300

Ser Tyr Met Asp Pro Met Asn Glu Tyr Asn Ala Leu Asn Glu Ala Lys
 305 310 315 320

Gln Met Ile Ala Val Ala Asp Glu Asn Gln Asn His His Leu Glu Pro
 325 330 335

Glu Glu Val Leu Lys Tyr Ser Glu Phe Phe Thr Gly Ser Lys Leu Val
 340 345 350

Asp Tyr Ala Arg Ser Val His Glu Glu Phe
 355 360

<210> 254

<211> 504

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 254

Met Val Ala Pro Gly Ser Val Thr Ser Arg Leu Gly Ser Val Phe Pro
 1 5 10 15

Phe Leu Leu Val Leu Val Asp Leu Gln Tyr Glu Gly Ala Glu Cys Gly
 20 25 30

Val Asn Ala Asp Val Glu Lys His Leu Glu Leu Gly Lys Lys Leu Leu
 35 40 45

Ala Ala Gly Gln Leu Ala Asp Ala Leu Ser Gln Phe His Ala Ala Val
 50 55 60

Asp Gly Asp Pro Asp Asn Tyr Ile Ala Tyr Tyr Arg Arg Ala Thr Val
 65 70 75 80

Phe Leu Ala Met Gly Lys Ser Lys Ala Ala Leu Pro Asp Leu Thr Lys
 85 90 95

Val Ile Gln Leu Lys Met Asp Phe Thr Ala Ala Arg Leu Gln Arg Gly
 100 105 110

His Leu Leu Leu Lys Gln Gly Lys Leu Asp Glu Ala Glu Asp Asp Phe
 115 120 125

Lys Lys Val Leu Lys Ser Asn Pro Ser Glu Asn Glu Glu Lys Glu Ala
 130 135 140

Gln Ser Gln Leu Ile Lys Ser Asp Glu Met Gln Arg Leu Arg Ser Gln
 145 150 155 160

Ala Leu Asn Ala Phe Gly Ser Gly Asp Tyr Thr Ala Ala Ile Ala Phe
 165 170 175

Leu Asp Lys Ile Leu Glu Val Cys Val Trp Asp Ala Glu Leu Arg Glu
 180 185 190

Leu Arg Ala Glu Cys Phe Ile Lys Glu Gly Glu Pro Arg Lys Ala Ile
 195 200 205

Ser Asp Leu Lys Ala Ala Ser Lys Leu Lys Asn Asp Asn Thr Glu Ala
 210 215 220

Phe Tyr Lys Ile Ser Thr Leu Tyr Tyr Gln Leu Gly Asp His Glu Leu
 225 230 235 240

Protein Complexes associated with APP-processing

Ser Leu Ser Glu Val Arg Glu Cys Leu Lys Leu Asp Gln Asp His Lys
245 250 255

Arg Cys Phe Ala His Tyr Lys Gln Val Lys Lys Leu Asn Lys Leu Ile
260 265 270

Glu Ser Ala Glu Glu Leu Ile Arg Asp Gly Arg Tyr Thr Asp Ala Thr
275 280 285

Ser Lys Tyr Glu Ser Val Met Lys Thr Glu Pro Ser Ile Ala Glu Tyr
290 295 300

Thr Val Arg Ser Lys Glu Arg Ile Cys His Cys Phe Ser Lys Asp Glu
305 310 315 320

Lys Pro Val Glu Ala Ile Arg Val Cys Ser Glu Val Leu Gln Met Glu
325 330 335

Pro Asp Asn Val Asn Ala Leu Lys Asp Arg Ala Glu Ala Tyr Leu Ile
340 345 350

Glu Glu Met Tyr Asp Glu Ala Ile Gln Asp Tyr Glu Thr Ala Gln Glu
355 360 365

His Asn Glu Asn Asp Gln Gln Ile Arg Glu Gly Leu Glu Lys Ala Gln
370 375 380

Arg Leu Leu Lys Gln Ser Gln Lys Arg Asp Tyr Tyr Lys Ile Leu Gly
385 390 395 400

Val Lys Arg Asn Ala Lys Lys Gln Glu Ile Ile Lys Ala Tyr Arg Lys
405 410 415

Leu Ala Leu Gln Trp His Pro Asp Asn Phe Gln Asn Glu Glu Glu Lys
420 425 430

Lys Lys Ala Glu Lys Lys Phe Ile Asp Ile Ala Ala Ala Lys Glu Val
435 440 445

Leu Ser Asp Pro Glu Met Arg Lys Lys Phe Asp Asp Gly Glu Asp Pro
450 455 460

Leu Asp Ala Glu Ser Gln Gln Gly Gly Gly Gly Asn Pro Phe His Arg
465 470 475 480

Ser Trp Asn Ser Trp Gln Gly Phe Asn Pro Phe Ser Ser Gly Gly Pro
485 490 495

Phe Arg Phe Lys Phe His Phe Asn
500

Protein Complexes associated with APP-processing

<210> 255

<211> 1104

<212> PRT

<213> Homo sapiens

<400> 255

Met Glu Arg Ser Pro Gly Glu Gly Pro Ser Pro Ser Pro Met Asp Gln
 1 5 10 15

Pro Ser Ala Pro Ser Asp Pro Thr Asp Gln Pro Pro Ala Ala His Ala
 20 25 30

Lys Pro Asp Pro Gly Ser Gly Gly Gln Pro Ala Gly Pro Gly Ala Ala
 35 40 45

Gly Glu Ala Leu Ala Val Leu Thr Ser Phe Gly Arg Arg Leu Leu Val
 50 55 60

Leu Ile Pro Val Tyr Leu Ala Gly Ala Val Gly Leu Ser Val Gly Phe
 65 70 75 80

Val Leu Phe Gly Leu Ala Leu Tyr Leu Gly Trp Arg Arg Val Arg Asp
 85 90 95

Glu Lys Glu Arg Ser Leu Arg Ala Ala Arg Gln Leu Leu Asp Asp Glu
 100 105 110

Glu Gln Leu Thr Ala Lys Thr Leu Tyr Met Ser His Arg Glu Leu Pro
 115 120 125

Ala Trp Val Ser Phe Pro Asp Val Glu Lys Ala Glu Trp Leu Asn Lys
 130 135 140

Ile Val Ala Gln Val Trp Pro Phe Leu Gly Gln Tyr Met Glu Lys Leu
 145 150 155 160

Leu Ala Glu Thr Val Ala Pro Ala Val Arg Gly Ser Asn Pro His Leu
 165 170 175

Gln Thr Phe Thr Phe Thr Arg Val Glu Leu Gly Glu Lys Pro Leu Arg
 180 185 190

Ile Ile Gly Val Lys Val His Pro Gly Gln Arg Lys Glu Gln Ile Leu
 195 200 205

Leu Asp Leu Asn Ile Ser Tyr Val Gly Asp Val Gln Ile Asp Val Glu
 210 215 220

Protein Complexes associated with APP-processing

Val Lys Lys Tyr Phe Cys Lys Ala Gly Val Lys Gly Met Gln Leu His
 225 230 235 240

Gly Val Leu Arg Val Ile Leu Glu Pro Leu Ile Gly Asp Leu Pro Phe
 245 250 255

Val Gly Ala Val Ser Met Phe Phe Ile Arg Arg Pro Thr Leu Asp Ile
 260 265 270

Asn Trp Thr Gly Met Thr Asn Leu Leu Asp Ile Pro Gly Leu Ser Ser
 275 280 285

Leu Ser Asp Thr Met Ile Met Asp Ser Ile Ala Ala Phe Leu Val Leu
 290 295 300

Pro Asn Arg Leu Leu Val Pro Leu Val Pro Asp Leu Gln Asp Val Ala
 305 310 315 320

Gln Leu Arg Ser Pro Leu Pro Arg Gly Ile Ile Arg Ile His Leu Leu
 325 330 335

Ala Ala Arg Gly Leu Ser Ser Lys Asp Lys Tyr Val Lys Gly Leu Ile
 340 345 350

Glu Gly Lys Ser Asp Pro Tyr Ala Leu Val Arg Leu Gly Thr Gln Thr
 355 360 365

Phe Cys Ser Arg Val Ile Asp Glu Glu Leu Asn Pro Gln Trp Gly Glu
 370 375 380

Thr Tyr Glu Val Met Val His Glu Val Pro Gly Gln Glu Ile Glu Val
 385 390 395 400

Glu Val Phe Asp Lys Asp Pro Asp Lys Asp Asp Phe Leu Gly Arg Met
 405 410 415

Lys Leu Asp Val Gly Lys Val Leu Gln Ala Ser Val Leu Asp Asp Trp
 420 425 430

Phe Pro Leu Gln Gly Gly Gln Gly Gln Val His Leu Arg Leu Glu Trp
 435 440 445

Leu Ser Leu Leu Ser Asp Ala Glu Lys Leu Glu Gln Val Leu Gln Trp
 450 455 460

Asn Trp Gly Val Ser Ser Arg Pro Asp Pro Pro Ser Ala Ala Ile Leu
 465 470 475 480

Val Val Tyr Leu Asp Arg Ala Gln Asp Leu Pro Leu Lys Lys Gly Asn
 485 490 495

protein Complexes associated with APP-processing

Lys Glu Pro Asn Pro Met Val Gln Leu Ser Ile Gln Asp Val Thr Gln
500 505 510

Glu Ser Lys Ala Val Tyr Ser Thr Asn Cys Pro Val Trp Glu Glu Ala
515 520 525

Phe Arg Phe Phe Leu Gln Asp Pro Gln Ser Gln Glu Leu Asp Val Gln
530 535 540

Val Lys Asp Asp Ser Arg Ala Leu Thr Leu Gly Ala Leu Thr Leu Pro
545 550 555 560

Leu Ala Arg Leu Leu Thr Ala Pro Glu Leu Ile Leu Asp Gln Trp Phe
565 570 575

Gln Leu Ser Ser Ser Gly Pro Asn Ser Arg Leu Tyr Met Lys Leu Val
580 585 590

Met Arg Ile Leu Tyr Leu Asp Ser Ser Glu Ile Cys Phe Pro Thr Val
595 600 605

Pro Gly Cys Pro Gly Ala Trp Asp Val Asp Ser Glu Asn Pro Gln Arg
610 615 620

Gly Ser Ser Val Asp Ala Pro Pro Arg Pro Cys His Thr Thr Pro Asp
625 630 635 640

Ser Gln Phe Gly Thr Glu His Val Leu Arg Ile His Val Leu Glu Ala
645 650 655

Gln Asp Leu Ile Ala Lys Asp Arg Phe Leu Gly Gly Leu Val Lys Gly
660 665 670

Lys Ser Asp Pro Tyr Val Lys Leu Lys Leu Ala Gly Arg Ser Phe Arg
675 680 685

Ser His Val Val Arg Glu Asp Leu Asn Pro Arg Trp Asn Glu Val Phe
690 695 700

Glu Val Ile Val Thr Ser Val Pro Gly Gln Glu Leu Glu Val Glu Val
705 710 715 720

Phe Asp Lys Asp Leu Asp Lys Asp Asp Phe Leu Gly Arg Cys Lys Val
725 730 735

Arg Leu Thr Thr Val Leu Asn Ser Gly Phe Leu Asp Glu Trp Leu Thr
740 745 750

Leu Glu Asp Val Pro Ser Gly Arg Leu His Leu Arg Leu Glu Arg Leu
755 760 765

Protein Complexes associated with APP-processing

Thr Pro Arg Pro Thr Ala Ala Glu Leu Glu Glu Val Leu Gln Val Asn
770 775 780

Ser Leu Ile Gln Thr Gln Lys Ser Ala Glu Leu Ala Ala Ala Leu Leu
785 790 795 800

Ser Ile Tyr Met Glu Arg Ala Glu Asp Leu Pro Leu Arg Lys Gly Thr
805 810 815

Lys His Leu Ser Pro Tyr Ala Thr Leu Thr Val Gly Asp Ser Ser His
820 825 830

Lys Thr Lys Thr Ile Ser Gln Thr Ser Ala Pro Val Trp Asp Glu Ser
835 840 845

Ala Ser Phe Leu Ile Arg Lys Pro His Thr Glu Ser Leu Glu Leu Gln
850 855 860

Val Arg Gly Glu Gly Thr Gly Val Leu Gly Ser Leu Ser Leu Pro Leu
865 870 875 880

Ser Glu Leu Leu Val Ala Asp Gln Leu Cys Leu Asp Arg Trp Phe Thr
885 890 895

Leu Ser Ser Gly Gln Gly Gln Val Leu Leu Arg Ala Gln Leu Gly Ile
900 905 910

Leu Val Ser Gln His Ser Gly Val Glu Ala His Ser His Ser Tyr Ser
915 920 925

His Ser Ser Ser Ser Leu Ser Glu Glu Pro Glu Leu Ser Gly Gly Pro
930 935 940

Pro His Ile Thr Ser Ser Ala Pro Glu Leu Arg Gln Arg Leu Thr His
945 950 955 960

Val Asp Ser Pro Leu Glu Ala Pro Ala Gly Pro Leu Gly Gln Val Lys
965 970 975

Leu Thr Leu Trp Tyr Tyr Ser Glu Glu Arg Lys Leu Val Ser Ile Val
980 985 990

His Gly Cys Arg Ser Leu Arg Gln Asn Gly Arg Asp Pro Pro Asp Pro
995 1000 1005

Tyr Val Ser Leu Leu Leu Leu Pro Asp Lys Asn Arg Gly Thr Lys
1010 1015 1020

Arg Arg Thr Ser Gln Lys Lys Arg Thr Leu Ser Pro Glu Phe Asn
1025 1030 1035

Protein Complexes associated with APP-processing

Glu Arg Phe Glu Trp Glu Leu Pro Leu Asp Glu Ala Gln Arg Arg
 1040 1045 1050

Lys Leu Asp Val Ser Val Lys Ser Asn Ser Ser Phe Met Ser Arg
 1055 1060 1065

Glu Arg Glu Leu Leu Gly Lys Val Gln Leu Asp Leu Ala Glu Thr
 1070 1075 1080

Asp Leu Ser Gln Gly Val Ala Arg Trp Tyr Asp Leu Met Asp Asn
 1085 1090 1095

Lys Asp Lys Gly Ser Ser
 1100

<210> 256

<211> 1257

<212> PRT

<213> Homo sapiens

<400> 256

Met Val Val Ala Leu Arg Tyr Val Trp Pro Leu Leu Leu Cys Ser Pro
 1 5 10 15

Cys Leu Leu Ile Gln Ile Pro Glu Glu Tyr Glu Gly His His Val Met
 20 25 30

Glu Pro Pro Val Ile Thr Glu Gln Ser Pro Arg Arg Leu Val Val Phe
 35 40 45

Pro Thr Asp Asp Ile Ser Leu Lys Cys Glu Ala Ser Gly Lys Pro Glu
 50 55 60

Val Gln Phe Arg Trp Thr Arg Asp Gly Val His Phe Lys Pro Lys Glu
 65 70 75 80

Glu Leu Gly Val Thr Val Tyr Gln Ser Pro His Ser Gly Ser Phe Thr
 85 90 95

Ile Thr Gly Asn Asn Ser Asn Phe Ala Gln Arg Phe Gln Gly Ile Tyr
 100 105 110

Arg Cys Phe Ala Ser Asn Lys Leu Gly Thr Ala Met Ser His Glu Ile
 115 120 125

Arg Leu Met Ala Glu Gly Ala Pro Lys Trp Pro Lys Glu Thr Val Lys
 130 135 140

Protein Complexes associated with APP-processing
 Pro Val Glu Val Glu Glu Gly Glu Ser Val Val Leu Pro Cys Asn Pro
 145 150 155 160

Pro Pro Ser Ala Glu Pro Leu Arg Ile Tyr Trp Met Asn Ser Lys Ile
 165 170 175

Leu His Ile Lys Gln Asp Glu Arg Val Thr Met Gly Gln Asn Gly Asn
 180 185 190

Leu Tyr Phe Ala Asn Val Leu Thr Ser Asp Asn His Ser Asp Tyr Ile
 195 200 205

Cys His Ala His Phe Pro Gly Thr Arg Thr Ile Ile Gln Lys Glu Pro
 210 215 220

Ile Asp Leu Arg Val Lys Ala Thr Asn Ser Met Ile Asp Arg Lys Pro
 225 230 235 240

Arg Leu Leu Phe Pro Thr Asn Ser Ser Ser His Leu Val Ala Leu Gln
 245 250 255

Gly Gln Pro Leu Val Leu Glu Cys Ile Ala Glu Gly Phe Pro Thr Pro
 260 265 270

Thr Ile Lys Trp Leu Arg Pro Ser Gly Pro Met Pro Ala Asp Arg Val
 275 280 285

Thr Tyr Gln Asn His Asn Lys Thr Leu Gln Leu Leu Lys Val Gly Glu
 290 295 300

Glu Asp Asp Gly Glu Tyr Arg Cys Leu Ala Glu Asn Ser Leu Gly Ser
 305 310 315 320

Ala Arg His Ala Tyr Tyr Val Thr Val Glu Ala Ala Pro Tyr Trp Leu
 325 330 335

His Lys Pro Gln Ser His Leu Tyr Gly Pro Gly Glu Thr Ala Arg Leu
 340 345 350

Asp Cys Gln Val Gln Gly Arg Pro Gln Pro Glu Val Thr Trp Arg Ile
 355 360 365

Asn Gly Ile Pro Val Glu Glu Leu Ala Lys Asp Gln Lys Tyr Arg Ile
 370 375 380

Gln Arg Gly Ala Leu Ile Leu Ser Asn Val Gln Pro Ser Asp Thr Met
 385 390 395 400

Val Thr Gln Cys Glu Ala Arg Asn Arg His Gly Leu Leu Leu Ala Asn
 405 410 415

Protein Complexes associated with APP-processing

Ala Tyr Ile Tyr Val Val Gln Leu Pro Ala Lys Ile Leu Thr Ala Asp
420 425 430

Asn Gln Thr Tyr Met Ala Val Gln Gly Ser Thr Ala Tyr Leu Leu Cys
435 440 445

Lys Ala Phe Gly Ala Pro Val Pro Ser Val Gln Trp Leu Asp Glu Asp
450 455 460

Gly Thr Thr Val Leu Gln Asp Glu Arg Phe Phe Pro Tyr Ala Asn Gly
465 470 475 480

Thr Leu Gly Ile Arg Asp Leu Gln Ala Asn Asp Thr Gly Arg Tyr Phe
485 490 495

Cys Leu Ala Ala Asn Asp Gln Asn Asn Val Thr Ile Met Ala Asn Leu
500 505 510

Lys Val Lys Asp Ala Thr Gln Ile Thr Gln Gly Pro Arg Ser Thr Ile
515 520 525

Glu Lys Lys Gly Ser Arg Val Thr Phe Thr Cys Gln Ala Ser Phe Asp
530 535 540

Pro Ser Leu Gln Pro Ser Ile Thr Trp Arg Gly Asp Gly Arg Asp Leu
545 550 555 560

Gln Glu Leu Gly Asp Ser Asp Lys Tyr Phe Ile Glu Asp Gly Arg Leu
565 570 575

Val Ile His Ser Leu Asp Tyr Ser Asp Gln Gly Asn Tyr Ser Cys Val
580 585 590

Ala Ser Thr Glu Leu Asp Val Val Glu Ser Arg Ala Gln Leu Leu Val
595 600 605

Val Gly Ser Pro Gly Pro Val Pro Arg Leu Val Leu Ser Asp Leu His
610 615 620

Leu Leu Thr Gln Ser Gln Val Arg Val Ser Trp Ser Pro Ala Glu Asp
625 630 635 640

His Asn Ala Pro Ile Glu Lys Tyr Asp Ile Glu Phe Glu Asp Lys Glu
645 650 655

Met Ala Pro Glu Lys Trp Tyr Ser Leu Gly Lys Val Pro Gly Asn Gln
660 665 670

Thr Ser Thr Thr Leu Lys Leu Ser Pro Tyr Val His Tyr Thr Phe Arg
675 680 685

Protein Complexes associated with APP-processing

Val Lys Gly Glu Gly Asn Glu Thr Thr Asn Met Val Ile Thr Trp Lys
725 730 735

Gln Trp Arg Pro Gln Gly Thr Arg Gly Pro Trp Gln Glu Gln Ile Val
755 760 765

Glu Ile Lys Val Gln Ala Val Asn Ser Gln Gly Lys Gly Pro Glu Pro
785 790 795 800

Glu Leu Glu Gly Ile Glu Ile Leu Asn Ser Ser Ala Val Leu Val Lys
820 825 830

Asn Val Thr Tyr Trp Arg Glu Gly Ser Gln Arg Lys His Ser Lys Arg
850 855 860

Ile Leu Ser Gly Leu Arg Pro Tyr Ser Ser Tyr His Leu Glu Val Gln
885 890 895

Thr Pro Glu Gly Val Pro Gly His Pro Glu Ala Leu His Leu Glu Cys
915 920 925

Asn Gly Val Leu Thr Gly Tyr Val Leu Ser Tyr His Pro Leu Asp Glu
945 950 955 960

Protein Complexes associated with APP-processing
 Gly Gly Lys Gly Gln Leu Ser Phe Asn Leu Arg Asp Pro Glu Leu Arg
 965 970 975

Thr His Asn Leu Thr Asp Leu Ser Pro His Leu Arg Tyr Arg Phe Gln
 980 985 990

Leu Gln Ala Thr Thr Lys Glu Gly Pro Gly Glu Ala Ile Val Arg Glu
 995 1000 1005

Gly Gly Thr Met Ala Leu Ser Gly Ile Ser Asp Phe Gly Asn Ile
 1010 1015 1020

Ser Ala Thr Ala Gly Glu Asn Tyr Ser Val Val Ser Trp Val Pro
 1025 1030 1035

Lys Glu Gly Gln Cys Asn Phe Arg Phe His Ile Leu Phe Lys Ala
 1040 1045 1050

Leu Gly Glu Glu Lys Gly Gly Ala Ser Leu Ser Pro Gln Tyr Val
 1055 1060 1065

Ser Tyr Asn Gln Ser Ser Tyr Thr Gln Trp Asp Leu Gln Pro Asp
 1070 1075 1080

Thr Asp Tyr Glu Ile His Leu Phe Lys Glu Arg Met Phe Arg His
 1085 1090 1095

Gln Met Ala Val Lys Thr Asn Gly Thr Gly Arg Val Arg Leu Pro
 1100 1105 1110

Pro Ala Gly Phe Ala Thr Glu Gly Trp Phe Ile Gly Phe Val Ser
 1115 1120 1125

Ala Ile Ile Leu Leu Leu Leu Val Leu Leu Ile Leu Cys Phe Ile
 1130 1135 1140

Lys Arg Ser Lys Gly Gly Lys Tyr Ser Val Lys Asp Lys Glu Asp
 1145 1150 1155

Thr Gln Val Asp Ser Glu Ala Arg Pro Met Lys Asp Glu Thr Phe
 1160 1165 1170

Gly Glu Tyr Arg Ser Leu Glu Ser Asp Asn Glu Glu Lys Ala Phe
 1175 1180 1185

Gly Ser Ser Gln Pro Ser Leu Asn Gly Asp Ile Lys Pro Leu Gly
 1190 1195 1200

Ser Asp Asp Ser Leu Ala Asp Tyr Gly Gly Ser Val Asp Val Gln
 1205 1210 1215

Protein Complexes associated with APP-processing
 Phe Asn Glu Asp Gly Ser Phe Ile Gly Gln Tyr Ser Gly Lys Lys
 1220 1225 1230

Glu Lys Glu Ala Ala Gly Gly Asn Asp Ser Ser Gly Ala Thr Ser
 1235 1240 1245

Pro Ile Asn Pro Ala Val Ala Leu Glu
 1250 1255

<210> 257

<211> 800

<212> PRT

<213> Homo sapiens

<400> 257

Met Ala Val Arg Glu Leu Cys Phe Pro Arg Gln Arg Gln Val Leu Phe
 1 5 10 15

Leu Phe Leu Phe Trp Gly Val Ser Leu Ala Gly Ser Gly Phe Gly Arg
 20 25 30

Tyr Ser Val Thr Glu Glu Thr Glu Lys Gly Ser Phe Val Val Asn Leu
 35 40 45

Ala Lys Asp Leu Gly Leu Ala Glu Gly Glu Leu Ala Ala Arg Gly Thr
 50 55 60

Arg Val Val Ser Asp Asp Asn Lys Gln Tyr Leu Leu Leu Asp Ser His
 65 70 75 80

Thr Gly Asn Leu Leu Thr Asn Glu Lys Leu Asp Arg Glu Lys Leu Cys
 85 90 95

Gly Pro Lys Glu Pro Cys Met Leu Tyr Phe Gln Ile Leu Met Asp Asp
 100 105 110

Pro Phe Gln Ile Tyr Arg Ala Glu Leu Arg Val Arg Asp Ile Asn Asp
 115 120 125

His Ala Pro Val Phe Gln Asp Lys Glu Thr Val Leu Lys Ile Ser Glu
 130 135 140

Asn Thr Ala Glu Gly Thr Ala Phe Arg Leu Glu Arg Ala Gln Asp Pro
 145 150 155 160

Asp Gly Gly Leu Asn Gly Ile Gln Asn Tyr Thr Ile Ser Pro Asn Ser
 165 170 175

Protein Complexes associated with APP-processing

Phe Phe His Ile Asn Ile Ser Gly Gly Asp Glu Gly Met Ile Tyr Pro
 180 185 190

Glu Leu Val Leu Asp Lys Ala Leu Asp Arg Glu Glu Gln Gly Glu Leu
 195 200 205

Ser Leu Thr Leu Thr Ala Leu Asp Gly Gly Ser Pro Ser Arg Ser Gly
 210 215 220

Thr Ser Thr Val Arg Ile Val Val Leu Asp Val Asn Asp Asn Ala Pro
 225 230 235 240

Gln Phe Ala Gln Ala Leu Tyr Glu Thr Gln Ala Pro Glu Asn Ser Pro
 245 250 255

Ile Gly Phe Leu Ile Val Lys Val Trp Ala Glu Asp Val Asp Ser Gly
 260 265 270

Val Asn Ala Glu Val Ser Tyr Ser Phe Phe Asp Ala Ser Glu Asn Ile
 275 280 285

Arg Thr Thr Phe Gln Ile Asn Pro Phe Ser Gly Glu Ile Phe Leu Arg
 290 295 300

Glu Leu Leu Asp Tyr Glu Leu Val Asn Ser Tyr Lys Ile Asn Ile Gln
 305 310 315 320

Ala Met Asp Gly Gly Gly Leu Ser Ala Arg Cys Arg Val Leu Val Glu
 325 330 335

Val Leu Asp Thr Asn Asp Asn Pro Pro Glu Leu Ile Val Ser Ser Phe
 340 345 350

Ser Asn Ser Val Ala Glu Asn Ser Pro Glu Thr Pro Leu Ala Val Phe
 355 360 365

Lys Ile Asn Asp Arg Asp Ser Gly Glu Asn Gly Lys Met Val Cys Tyr
 370 375 380

Ile Gln Glu Asn Leu Pro Phe Leu Leu Lys Pro Ser Val Glu Asn Phe
 385 390 395 400

Tyr Ile Leu Ile Thr Glu Gly Ala Leu Asp Arg Glu Ile Arg Ala Glu
 405 410 415

Tyr Asn Ile Thr Ile Thr Val Thr Asp Leu Gly Thr Pro Arg Leu Lys
 420 425 430

Thr Glu His Asn Ile Thr Val Leu Val Ser Asp Val Asn Asp Asn Ala
 435 440 445

Protein Complexes associated with APP-processing

Pro Ala Phe Thr Gln Thr Ser Tyr Thr Leu Phe Val Arg Glu Asn Asn
 450 455 460

Ser Pro Ala Leu His Ile Gly Ser Val Ser Ala Thr Asp Arg Asp Ser
 465 470 475 480

Gly Thr Asn Ala Gln Val Thr Tyr Ser Leu Leu Pro Pro Gln Asp Pro
 485 490 495

His Leu Pro Leu Ala Ser Leu Val Ser Ile Asn Ala Asp Asn Gly His
 500 505 510

Leu Phe Ala Leu Arg Ser Leu Asp Tyr Glu Ala Leu Gln Ala Phe Glu
 515 520 525

Phe Arg Val Gly Ala Thr Asp Arg Gly Ser Pro Ala Leu Ser Arg Glu
 530 535 540

Ala Leu Val Arg Val Leu Val Leu Asp Ala Asn Asp Asn Ser Pro Phe
 545 550 555 560

Val Leu Tyr Pro Leu Gln Asn Gly Ser Ala Pro Cys Thr Glu Leu Val
 565 570 575

Pro Arg Ala Ala Glu Pro Gly Tyr Leu Val Thr Lys Val Val Ala Val
 580 585 590

Asp Gly Asp Ser Gly Gln Asn Ala Trp Leu Ser Tyr Gln Leu Leu Lys
 595 600 605

Ala Thr Glu Pro Gly Leu Phe Gly Val Trp Ala His Asn Gly Glu Val
 610 615 620

Arg Thr Ala Arg Leu Leu Ser Glu Arg Asp Ala Ala Lys His Arg Leu
 625 630 635 640

Val Val Leu Val Lys Asp Asn Gly Glu Pro Pro Arg Ser Ala Thr Ala
 645 650 655

Thr Leu His Leu Leu Leu Val Asp Gly Phe Ser Gln Pro Tyr Leu Pro
 660 665 670

Leu Pro Glu Ala Ala Pro Ala Gln Ala Gln Ala Glu Ala Asp Leu Leu
 675 680 685

Thr Val Tyr Leu Val Val Ala Leu Ala Ser Val Ser Ser Leu Phe Leu
 690 695 700

Leu Ser Val Leu Leu Phe Val Ala Val Arg Leu Cys Arg Arg Ser Arg
 705 710 715 720

Protein Complexes associated with APP-processing
 Ala Ala Ser Val Gly Arg Cys Ser Val Pro Glu Gly Pro Phe Pro Gly
 725 730 735

His Leu Val Asp Val Arg Gly Ala Glu Thr Leu Ser Gln Ser Tyr Gln
 740 745 750

Tyr Glu Val Cys Leu Thr Gly Gly Pro Gly Thr Ser Glu Phe Lys Phe
 755 760 765

Leu Lys Pro Val Ile Ser Asp Ile Gln Ala Gln Gly Pro Gly Arg Lys
 770 775 780

Gly Glu Glu Asn Ser Thr Phe Arg Asn Ser Phe Gly Phe Asn Ile Gln
 785 790 795 800

<210> 258

<211> 798

<212> PRT

<213> Homo sapiens

<400> 258

Met Glu Ile Arg Gly Ala Leu Asp Leu Arg Lys Arg Gln Val Leu Ile
 1 5 10 15

Phe Leu Val Leu Leu Gly Leu Ser Arg Ala Gly Thr Glu Ser Ala His
 20 25 30

Tyr Ser Val Ala Glu Glu Thr Glu Ile Gly Ser Phe Val Ala Asn Leu
 35 40 45

Ala Arg Asp Leu Gly Leu Gly Val Glu Glu Leu Ser Ser Arg Glu Ala
 50 55 60

Arg Val Val Ser Asp Asp Asn Lys Lys Tyr Leu His Leu Asp Leu Leu
 65 70 75 80

Thr Gly Asn Leu Leu Leu Asn Glu Lys Leu Asp Arg Asp Glu Leu Cys
 85 90 95

Gly Ser Thr Glu Pro Cys Val Leu His Phe Gln Val Val Leu Glu Asn
 100 105 110

Pro Leu Gln Phe Phe Arg Phe Glu Leu Cys Val Lys Asp Ile Asn Asp
 115 120 125

His Ser Pro Thr Phe Leu Asp Lys Glu Ile Leu Ile Lys Ile Ser Glu
 130 135 140

Protein Complexes associated with APP-processing
 Gly Thr Thr Val Gly Ala Thr Phe Leu Met Glu Ser Ala Gln Asp Leu
 145 150 155 160

Asp Val Gly Ser Asn Ser Leu Gln Asn Tyr Thr Ile Ser Pro Asn Ser
 165 170 175

His Phe Tyr Ile Lys Ile Pro Asp Ser Ser Asp Arg Lys Ile Tyr Pro
 180 185 190

Glu Leu Val Leu Asp Arg Ala Leu Asp Tyr Glu Gln Glu Ala Glu Leu
 195 200 205

Arg Leu Thr Leu Thr Ala Val Asp Gly Gly Ser Pro Pro Lys Ser Gly
 210 215 220

Thr Thr Leu Val Leu Ile Lys Val Leu Asp Ile Asn Asp Asn Ala Pro
 225 230 235 240

Glu Phe Pro Gln Ser Leu Tyr Glu Val Gln Val Pro Glu Asp Arg Pro
 245 250 255

Leu Gly Ser Trp Ile Ala Thr Ile Ser Ala Lys Asp Leu Asp Ala Gly
 260 265 270

Asn Tyr Gly Lys Ile Ser Tyr Thr Phe Phe His Ala Ser Glu Asp Ile
 275 280 285

Arg Lys Thr Phe Glu Ile Asn Pro Ile Ser Gly Glu Val Asn Leu Arg
 290 295 300

Ser Pro Leu Asp Phe Glu Val Ile Gln Ser Tyr Thr Ile Asn Ile Gln
 305 310 315 320

Ala Thr Asp Gly Gly Gly Leu Ser Gly Lys Cys Thr Leu Leu Val Lys
 325 330 335

Val Met Asp Ile Asn Asp Asn Pro Pro Glu Val Thr Ile Ser Ser Ile
 340 345 350

Thr Lys Arg Ile Pro Glu Asn Ala Ser Glu Thr Leu Val Ala Leu Phe
 355 360 365

Ser Ile Leu Asp Gln Asp Ser Gly Asp Asn Gly Arg Met Ile Cys Ser
 370 375 380

Ile Gln Asp Asn Leu Pro Phe Phe Leu Lys Pro Thr Phe Lys Asn Phe
 385 390 395 400

Phe Thr Leu Val Ser Glu Lys Ala Leu Asp Arg Glu Ser Gln Ala Glu
 405 410 415

Protein Complexes associated with APP-processing

Tyr Asn Ile Thr Ile Thr Val Thr Asp Leu Gly Thr Pro Arg Leu Lys
 420 425 430

Thr Glu Tyr Asn Ile Thr Val Leu Leu Ser Asp Val Asn Asp Asn Ala
 435 440 445

Pro Thr Phe Thr Gln Thr Ser Tyr Thr Leu Phe Val Arg Glu Asn Asn
 450 455 460

Ser Pro Ala Leu His Ile Gly Ser Val Ser Ala Thr Asp Arg Asp Ser
 465 470 475 480

Gly Thr Asn Ala Gln Val Asn Tyr Ser Leu Leu Pro Pro Gln Asp Arg
 485 490 495

His Leu Pro Leu Ala Ser Leu Val Ser Ile Asn Ala Asp Asn Gly His
 500 505 510

Leu Phe Ala Leu Arg Ser Leu Asp Tyr Glu Ala Leu Gln Glu Phe Glu
 515 520 525

Phe Arg Val Gly Ala Thr Asp Arg Gly Ser Pro Ala Leu Ser Ser Glu
 530 535 540

Ala Leu Val Arg Val Leu Val Leu Asp Ala Asn Asp Asn Ser Pro Phe
 545 550 555 560

Val Leu Tyr Pro Leu Gln Asn Gly Ser Ala Pro Cys Thr Glu Leu Val
 565 570 575

Pro Arg Ala Ala Glu Pro Gly Tyr Leu Val Thr Lys Val Val Ala Val
 580 585 590

Asp Gly Asp Ser Gly Gln Asn Ala Trp Leu Ser Tyr Gln Leu Leu Lys
 595 600 605

Ala Thr Glu Pro Gly Leu Phe Gly Val Trp Ala His Asn Gly Glu Val
 610 615 620

Arg Thr Ala Arg Leu Leu Ser Glu Arg Asp Ala Ala Lys His Arg Leu
 625 630 635 640

Val Val Leu Val Lys Asp Asn Gly Glu Pro Pro Arg Ser Ala Thr Ala
 645 650 655

Thr Leu His Val Leu Leu Val Asp Gly Phe Ser Gln Pro Tyr Leu Pro
 660 665 670

Leu Pro Glu Ala Ala Pro Ala Gln Ala Gln Ala Asp Ser Leu Thr Val
 675 680 685

Protein Complexes associated with APP-processing
 Tyr Leu Val Val Ala Leu Ala Ser Val Ser Ser Leu Phe Leu Phe Ser
 690 695 700

Val Leu Leu Phe Val Ala Val Arg Leu Cys Arg Arg Ser Arg Ala Ala
 705 710 715 720

Ser Val Gly Arg Cys Ser Val Pro Glu Gly Pro Phe Pro Gly His Leu
 725 730 735

Val Asp Val Ser Gly Thr Gly Thr Leu Ser Gln Ser Tyr Gln Tyr Glu
 740 745 750

Val Cys Leu Thr Gly Gly Ser Gly Thr Asn Glu Phe Lys Phe Leu Lys
 755 760 765

Pro Ile Ile Pro Asn Phe Gln Val His Asp Thr Gly Arg Asn Met Gly
 770 775 780

Glu Ile Glu Asn Phe Arg Asn Ser Phe Gly Leu Asn Ile Gln
 785 790 795

<210> 259

<211> 793

<212> PRT

<213> Homo sapiens

<400> 259

Met Glu Ala Arg Val Glu Arg Ala Val Gln Lys Arg Gln Val Leu Phe
 1 5 10 15

Leu Cys Val Phe Leu Gly Met Ser Trp Ala Gly Ala Glu Pro Leu Arg
 20 25 30

Tyr Phe Val Ala Glu Glu Thr Glu Arg Gly Thr Phe Leu Thr Asn Leu
 35 40 45

Ala Lys Asp Leu Gly Leu Gly Val Gly Glu Leu Arg Ala Arg Gly Thr
 50 55 60

Arg Ile Val Ser Asp Gln Asn Met Gln Ile Leu Leu Leu Ser Ser Leu
 65 70 75 80

Thr Gly Asp Leu Leu Leu Asn Glu Lys Leu Asp Arg Glu Glu Leu Cys
 85 90 95

Gly Pro Arg Glu Pro Cys Val Leu Pro Phe Gln Leu Leu Leu Glu Lys
 100 105 110

Protein Complexes associated with APP-processing

Pro Phe Gln Ile Phe Arg Ala Glu Leu Trp Val Arg Asp Ile Asn Asp
 115 120 125

His Ala Pro Val Phe Leu Asp Arg Glu Ile Ser Leu Lys Ile Leu Glu
 130 135 140

Ser Thr Thr Pro Gly Ala Ala Phe Leu Leu Glu Ser Ala Gln Asp Ser
 145 150 155 160

Asp Val Gly Thr Asn Ser Leu Ser Asn Tyr Thr Ile Ser Pro Asn Ala
 165 170 175

Tyr Phe His Ile Asn Val His Asp Ser Gly Glu Gly Asn Ile Tyr Pro
 180 185 190

Glu Leu Val Leu Asn Gln Val Leu Asp Arg Glu Glu Ile Pro Glu Phe
 195 200 205

Ser Leu Thr Leu Thr Ala Leu Asp Gly Gly Ser Pro Pro Arg Ser Gly
 210 215 220

Thr Ala Leu Val Arg Ile Leu Val Leu Asp Val Asn Asp Asn Ala Pro
 225 230 235 240

Asp Phe Val Arg Ser Leu Tyr Lys Val Gln Val Pro Glu Asn Ser Pro
 245 250 255

Val Gly Ser Met Val Val Ser Val Ser Ala Arg Asp Leu Asp Thr Gly
 260 265 270

Ser Asn Gly Glu Ile Ala Tyr Ala Phe Ser Tyr Ala Thr Glu Arg Ile
 275 280 285

Leu Lys Thr Phe Gln Ile Asn Pro Thr Ser Gly Ser Leu His Leu Lys
 290 295 300

Ala Gln Leu Asp Tyr Glu Ala Ile Gln Thr Tyr Thr Leu Thr Ile Gln
 305 310 315 320

Ala Lys Asp Gly Gly Gly Leu Ser Gly Lys Cys Thr Val Val Val Asp
 325 330 335

Val Thr Asp Ile Asn Asp Asn Arg Pro Glu Leu Leu Leu Ser Ser Leu
 340 345 350

Thr Ser Pro Ile Ala Glu Asn Ser Pro Glu Thr Val Val Ala Val Phe
 355 360 365

Arg Ile Arg Asp Arg Asp Ser Gly Asn Asn Gly Lys Thr Val Cys Ser
 370 375 380

Protein Complexes associated with APP-processing

Ile Gln Asp Asp Val Pro Phe Ile Leu Lys Pro Ser Val Glu Asn Phe
 385 390 395 400

Tyr Thr Leu Val Thr Glu Lys Pro Leu Asp Arg Glu Arg Asn Thr Glu
 405 410 415

Tyr Asn Ile Thr Ile Thr Val Thr Asp Leu Gly Thr Pro Arg Leu Lys
 420 425 430

Thr Glu His Asn Ile Thr Val Leu Val Ser Asp Val Asn Asp Asn Ala
 435 440 445

Pro Ala Phe Thr Gln Thr Ser Tyr Thr Leu Phe Val Arg Glu Asn Asn
 450 455 460

Ser Pro Ala Leu Pro Ile Gly Ser Val Ser Ala Thr Asp Arg Asp Ser
 465 470 475 480

Gly Thr Asn Ala Gln Val Ile Tyr Ser Leu Leu Pro Ser Gln Asp Pro
 485 490 495

His Leu Pro Leu Ala Ser Leu Val Ser Ile Asn Ala Asp Asn Gly His
 500 505 510

Leu Phe Ala Leu Arg Ser Leu Asp Tyr Glu Ala Leu Gln Ala Phe Glu
 515 520 525

Phe Arg Val Gly Ala Thr Asp Arg Gly Ser Pro Ala Leu Ser Ser Glu
 530 535 540

Ala Leu Val Arg Val Leu Val Leu Asp Ala Asn Asp Asn Ser Pro Phe
 545 550 555 560

Val Leu Tyr Pro Leu Gln Asn Ser Ser Ala Pro Cys Thr Glu Pro Leu
 565 570 575

Pro Arg Ala Ala Glu Pro Gly Tyr Leu Val Thr Lys Val Val Ala Val
 580 585 590

Asp Gly Asp Ser Gly Gln Asn Ala Trp Leu Ser Tyr Gln Leu Leu Lys
 595 600 605

Ala Thr Glu Pro Gly Leu Phe Gly Val Trp Ala His Asn Gly Glu Val
 610 615 620

Arg Thr Ala Arg Leu Leu Ser Glu Arg Asp Ala Ala Lys Gln Arg Leu
 625 630 635 640

Val Val Leu Val Lys Asp Asn Gly Glu Pro Pro Arg Ser Ala Thr Ala
 645 650 655

Protein Complexes associated with APP-processing
 Thr Leu His Val Leu Leu Val Asp Gly Phe Ser Gln Pro Tyr Leu Arg
 660 665 670

Leu Pro Glu Ala Ala Pro Asp Gln Ala Asn Ser Leu Thr Val Tyr Leu
 675 680 685

Val Val Ala Leu Ala Ser Val Ser Ser Leu Phe Leu Leu Ser Val Leu
 690 695 700

Leu Phe Val Ala Val Arg Leu Cys Arg Arg Ser Arg Ala Ala Pro Val
 705 710 715 720

Gly Arg Cys Ser Val Pro Glu Gly Pro Phe Pro Arg His Leu Val Asp
 725 730 735

Leu Ser Gly Thr Gly Thr Leu Ser Gln Ser Tyr Gln Tyr Glu Val Cys
 740 745 750

Leu Thr Gly Gly Ser Gly Thr Asn Glu Phe Lys Phe Leu Lys Pro Ile
 755 760 765

Ile Pro Asn Leu Leu Pro Gln Ser Thr Gly Arg Glu Val Glu Glu Asn
 770 775 780

Arg Pro Phe Gln Asn Asn Leu Gly Phe
 785 790

<210> 260

<211> 794

<212> PRT

<213> Homo sapiens

<400> 260

Met Arg Val Arg Ile Gly Leu Thr Leu Leu Leu Cys Ala Val Leu Leu
 1 5 10 15

Ser Leu Ala Ser Ala Ser Ser Asp Glu Glu Gly Ser Gln Asp Glu Ser
 20 25 30

Leu Asp Ser Lys Thr Thr Leu Thr Ser Asp Glu Ser Val Lys Asp His
 35 40 45

Thr Thr Ala Gly Arg Val Val Ala Gly Gln Ile Phe Leu Asp Ser Glu
 50 55 60

Glu Ser Glu Leu Glu Ser Ser Ile Gln Glu Glu Glu Asp Ser Leu Lys
 65 70 75 80

Val Gln Arg Ile Arg Leu Pro Asp Glu Val Glu Asn Pro Gly Met Asn
340 345 350

Protein Complexes associated with APP-processing
 Ser Gly Met Leu Glu Glu Asp Leu Ile Gln Tyr Tyr Gln Phe Leu Ala
 355 360 365

Glu Lys Gly Asp Val Gln Ala Gln Val Gly Leu Gly Gln Leu His Leu
 370 375 380

His Gly Gly Arg Gly Val Glu Gln Asn His Gln Arg Ala Phe Asp Tyr
 385 390 395 400

Phe Asn Leu Ala Ala Asn Ala Gly Asn Ser His Ala Met Ala Phe Leu
 405 410 415

Gly Lys Met Tyr Ser Glu Gly Ser Asp Ile Val Pro Gln Ser Asn Glu
 420 425 430

Thr Ala Leu His Tyr Phe Lys Lys Ala Ala Asp Met Gly Asn Pro Val
 435 440 445

Gly Gln Ser Gly Leu Gly Met Ala Tyr Leu Tyr Gly Arg Gly Val Gln
 450 455 460

Val Asn Tyr Asp Leu Ala Leu Lys Tyr Phe Gln Lys Ala Ala Glu Gln
 465 470 475 480

Gly Trp Val Asp Gly Gln Leu Gln Leu Gly Ser Met Tyr Tyr Asn Gly
 485 490 495

Ile Gly Val Lys Arg Asp Tyr Lys Gln Ala Leu Lys Tyr Phe Asn Leu
 500 505 510

Ala Ser Gln Gly Gly His Ile Leu Ala Phe Tyr Asn Leu Ala Gln Met
 515 520 525

His Ala Ser Gly Thr Gly Val Met Arg Ser Cys His Thr Ala Val Glu
 530 535 540

Leu Phe Lys Asn Val Cys Glu Arg Gly Arg Trp Ser Glu Arg Leu Met
 545 550 555 560

Thr Ala Tyr Asn Ser Tyr Lys Asp Gly Asp Tyr Asn Ala Ala Val Ile
 565 570 575

Gln Tyr Leu Leu Leu Ala Glu Gln Gly Tyr Glu Val Ala Gln Ser Asn
 580 585 590

Ala Ala Phe Ile Leu Asp Gln Arg Glu Ala Ser Ile Val Gly Glu Asn
 595 600 605

Glu Thr Tyr Pro Arg Ala Leu Leu His Trp Asn Arg Ala Ala Ser Gln
 610 615 620

Protein Complexes associated with APP-processing
 Gly Tyr Thr Val Ala Arg Ile Lys Leu Gly Asp Tyr His Phe Tyr Gly
 625 630 635 640

Phe Gly Thr Asp Val Asp Tyr Glu Thr Ala Phe Ile His Tyr Arg Leu
 645 650 655

Ala Ser Glu Gln Gln His Ser Ala Gln Ala Met Phe Asn Leu Gly Tyr
 660 665 670

Met His Glu Lys Gly Leu Gly Ile Lys Gln Asp Ile His Leu Ala Lys
 675 680 685

Arg Phe Tyr Asp Met Ala Ala Glu Ala Ser Pro Asp Ala Gln Val Pro
 690 695 700

Val Phe Leu Ala Leu Cys Lys Leu Gly Val Val Tyr Phe Leu Gln Tyr
 705 710 715 720

Ile Arg Glu Thr Asn Ile Arg Asp Met Phe Thr Gln Leu Asp Met Asp
 725 730 735

Gln Leu Leu Gly Pro Glu Trp Asp Leu Tyr Leu Met Thr Ile Ile Ala
 740 745 750

Leu Leu Leu Gly Thr Val Ile Ala Tyr Arg Gln Arg Gln His Gln Asp
 755 760 765

Met Pro Ala Pro Arg Pro Pro Gly Pro Arg Pro Ala Pro Pro Gln Gln
 770 775 780

Glu Gly Pro Pro Glu Gln Gln Pro Pro Gln
 785 790

<210> 261

<211> 464

<212> PRT

<213> Homo sapiens

<400> 261

Met Ser Thr Glu Lys Val Asp Gln Lys Glu Glu Ala Gly Glu Lys Glu
 1 5 10 15

Val Cys Gly Asp Gln Ile Lys Gly Pro Asp Lys Glu Glu Glu Pro Pro
 20 25 30

Ala Ala Ala Ser His Gly Gln Gly Trp Arg Pro Gly Gly Arg Ala Ala
 35 40 45

Protein Complexes associated with APP-processing

Arg Asn Ala Arg Pro Glu Pro Gly Ala Arg His Pro Ala Leu Pro Ala
50 55 60

Met Val Asn Asp Pro Pro Val Pro Ala Leu Leu Trp Ala Gln Glu Val
65 70 75 80

Gly Gln Val Leu Ala Gly Arg Ala Arg Arg Leu Leu Leu Gln Phe Gly
85 90 95

Val Leu Phe Cys Thr Ile Leu Leu Leu Leu Trp Val Ser Val Phe Leu
100 105 110

Tyr Gly Ser Phe Tyr Tyr Ser Tyr Met Pro Thr Val Ser His Leu Ser
115 120 125

Pro Val His Phe Tyr Tyr Arg Thr Asp Cys Asp Ser Ser Thr Thr Ser
130 135 140

Leu Cys Ser Phe Pro Val Ala Asn Val Ser Leu Thr Lys Gly Gly Arg
145 150 155 160

Asp Arg Val Leu Met Tyr Gly Gln Pro Tyr Arg Val Thr Leu Glu Leu
165 170 175

Glu Leu Pro Glu Ser Pro Val Asn Gln Asp Leu Gly Met Phe Leu Val
180 185 190

Thr Ile Ser Cys Tyr Thr Arg Gly Gly Arg Ile Ile Ser Thr Ser Ser
195 200 205

Arg Ser Val Met Leu His Tyr Arg Ser Asp Leu Leu Gln Met Leu Asp
210 215 220

Thr Leu Val Phe Ser Ser Leu Leu Leu Phe Gly Phe Ala Glu Gln Lys
225 230 235 240

Gln Leu Leu Glu Val Glu Leu Tyr Ala Asp Tyr Arg Glu Asn Ser Tyr
245 250 255

Val Pro Thr Thr Gly Ala Ile Ile Glu Ile His Ser Lys Arg Ile Gln
260 265 270

Leu Tyr Gly Ala Tyr Leu Arg Ile His Ala His Phe Thr Gly Leu Arg
275 280 285

Tyr Leu Leu Tyr Asn Phe Pro Met Thr Cys Ala Phe Ile Gly Val Ala
290 295 300

Ser Asn Phe Thr Phe Leu Ser Val Ile Val Leu Phe Ser Tyr Met Gln
305 310 315 320

Protein Complexes associated with APP-processing

Asn Ile Arg Lys Arg Asp Asn Ser Arg Lys Glu Val Gln Arg Arg Ile
340 345 350

Ser Ala His Gln Pro Gly Ala Gly Pro Glu Gly Gln Glu Glu Ser Thr
355 360 365

Pro Gln Ser Asp Val Thr Glu Asp Gly Glu Ser Pro Glu Asp Pro Ser
370 375 380

Gly Thr Glu Gly Gln Leu Ser Glu Glu Glu Lys Pro Asp Gln Gln Pro
385 390 395 400

Leu Ser Gly Glu Glu Leu Glu Pro Glu Ala Ser Asp Gly Ser Gly
405 410 415

Ser Trp Glu Asp Ala Ala Leu Leu Thr Glu Ala Asn Leu Pro Ala Pro
420 425 430

Ala Pro Ala Ser Ala Ser Ala Pro Val Leu Glu Thr Leu Gly Ser Ser
435 440 445

Glu Pro Ala Gly Gly Ala Leu Arg Gln Arg Pro Thr Cys Ser Ser Ser
450 455 460

<210> 262

<211> 299

<212> PRT

<213> Homo sapiens

<400> 262

Ser Arg Val Leu Cys Trp Val Gln Thr Pro Val Arg Pro Gly Gly Phe
1 5 10 15

Leu Val Ser Gln Ala Arg Ala Ser His Ser Pro Ala Trp Val Cys Gly
20 25 30

Arg Pro Arg Pro Gln Arg Thr Arg Pro Pro Thr Leu Thr Cys Pro Leu
35 40 45

Ser Cys Pro Ser Pro Ile Pro Ala Pro Ser Leu Pro Ser Arg Cys Pro
50 55 60

Ser Pro His Pro Ala Ala Ser Ala Arg Leu Ser Pro Arg Ala Pro Pro
65 70 75 80

Protein Complexes associated with APP-processing

Thr Arg Pro Leu Phe Ser Gly Asn Arg Ser Phe Arg Ser Ala Arg Leu
85 90 95

Glu Ser Phe Trp Pro Asp Ser Ala Ala Ser Phe His Arg Pro Ser Leu
100 105 110

Leu Leu Pro Pro Cys Gly Ser Val Ala Asn Ile Phe Lys Gly Leu Val
115 120 125

Ile Leu Pro Glu Met Ser Leu Val Ile Arg Asn Leu Gln Arg Val Ile
130 135 140

Pro Ile Arg Arg Ala Pro Leu Arg Ser Lys Ile Glu Ile Val Arg Arg
145 150 155 160

Ile Leu Gly Val Gln Lys Phe Asp Leu Gly Ile Ile Cys Val Asp Asn
165 170 175

Lys Asn Ile Gln His Ile Asn Arg Ile Tyr Arg Asp Arg Asn Val Pro
180 185 190

Thr Asp Val Leu Ser Phe Pro Phe His Glu His Leu Lys Ala Gly Glu
195 200 205

Phe Pro Gln Pro Asp Phe Pro Asp Asp Tyr Asn Leu Gly Asp Ile Phe
210 215 220

Leu Gly Val Glu Tyr Ile Phe His Gln Cys Lys Glu Asn Glu Asp Tyr
225 230 235 240

Asn Asp Val Leu Thr Val Thr Ala Thr His Gly Leu Cys His Leu Leu
245 250 255

Gly Phe Thr His Gly Thr Glu Ala Glu Trp Gln Gln Met Phe Gln Lys
260 265 270

Glu Lys Ala Val Leu Asp Glu Leu Gly Arg Arg Thr Gly Thr Arg Leu
275 280 285

Gln Pro Leu Thr Arg Gly Leu Phe Gly Gly Ser
290 295

<210> 263

<211> 256

<212> PRT

<213> Homo sapiens

<400> 263

Protein Complexes associated with APP-processing

Met Gln Pro Ala Lys Glu Val Thr Lys Ala Ser Asp Gly Ser Leu Leu
 1 5 10 15

Gly Asp Leu Gly His Thr Pro Leu Ser Lys Lys Glu Gly Ile Lys Trp
 20 25 30

Gln Arg Pro Arg Leu Ser Arg Gln Ala Leu Met Arg Cys Cys Leu Val
 35 40 45

Lys Trp Ile Leu Ser Ser Thr Ala Pro Gln Gly Ser Asp Ser Ser Asp
 50 55 60

Ser Glu Leu Glu Leu Ser Thr Val Arg His Gln Pro Glu Gly Leu Asp
 65 70 75 80

Gln Leu Gln Ala Gln Thr Lys Phe Thr Lys Lys Glu Leu Gln Ser Leu
 85 90 95

Tyr Arg Gly Phe Lys Asn Glu Cys Pro Thr Gly Leu Val Asp Glu Asp
 100 105 110

Thr Phe Lys Leu Ile Tyr Ala Gln Phe Phe Pro Gln Gly Asp Ala Thr
 115 120 125

Thr Tyr Ala His Phe Leu Phe Asn Ala Phe Asp Ala Asp Gly Asn Gly
 130 135 140

Ala Ile His Phe Glu Asp Phe Val Val Gly Leu Ser Ile Leu Leu Arg
 145 150 155 160

Gly Thr Val His Glu Lys Leu Lys Trp Ala Phe Asn Leu Tyr Asp Ile
 165 170 175

Asn Lys Asp Gly Tyr Ile Thr Lys Glu Glu Met Leu Ala Ile Met Lys
 180 185 190

Ser Ile Tyr Asp Met Met Gly Arg His Thr Tyr Pro Ile Leu Arg Glu
 195 200 205

Asp Ala Pro Ala Glu His Val Glu Arg Phe Phe Glu Lys Met Asp Arg
 210 215 220

Asn Gln Asp Gly Val Val Thr Ile Glu Glu Phe Leu Glu Ala Cys Gln
 225 230 235 240

Lys Asp Glu Asn Ile Met Ser Ser Met Gln Leu Phe Glu Asn Val Ile
 245 250 255

<210> 264

<211> 872

Protein Complexes associated with APP-processing

<212> PRT

<213> Homo sapiens

<400> 264

Met Val Gln Lys Ser Arg Asn Gly Gly Val Tyr Pro Gly Pro Ser Gly
 1 5 10 15

Glu Lys Lys Leu Lys Val Gly Phe Val Gly Leu Asp Pro Gly Ala Pro
 20 25 30

Asp Ser Thr Arg Asp Gly Ala Leu Leu Ile Ala Gly Ser Glu Ala Pro
 35 40 45

Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
 50 55 60

Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
 65 70 75 80

Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
 85 90 95

Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
 100 105 110

Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
 115 120 125

Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
 130 135 140

Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
 145 150 155 160

Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
 165 170 175

Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
 180 185 190

Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
 195 200 205

Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
 210 215 220

Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
 225 230 235 240

Protein Complexes associated with APP-processing

Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
 245 250 255

Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp Gly Leu
 260 265 270

Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
 275 280 285

Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
 290 295 300

Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
 305 310 315 320

Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
 325 330 335

Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
 340 345 350

Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
 355 360 365

Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser Arg Leu
 370 375 380

Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu Arg Asn Leu Lys Ser Lys
 385 390 395 400

Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser Pro Ser
 405 410 415

Lys Gly Ser Pro Cys Arg Gly Pro Leu Cys Gly Cys Cys Pro Gly Arg
 420 425 430

Ser Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe Ser Ser Pro Arg
 435 440 445

Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr Val Arg
 450 455 460

Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser Lys Val
 465 470 475 480

Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln Ala Phe
 485 490 495

Arg Ile Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu Glu Ala Ser Leu
 500 505 510

Protein Complexes associated with APP-processing

Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu Phe Val
 515 520 525

Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile Arg Ala Val Cys
 530 535 540

Val Met Arg Phe Leu Val Ser Lys Arg Lys Phe Lys Glu Ser Leu Arg
 545 550 555 560

Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly His Leu
 565 570 575

Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Val Asp Gln Ile
 580 585 590

Val Gly Arg Gly Pro Ala Ile Thr Asp Lys Asp Arg Thr Lys Gly Pro
 595 600 605

Ala Glu Ala Glu Leu Pro Glu Asp Pro Ser Met Met Gly Arg Leu Gly
 610 615 620

Lys Val Glu Lys Gln Val Leu Ser Met Glu Lys Lys Leu Asp Phe Leu
 625 630 635 640

Val Asn Ile Tyr Met Gln Arg Met Gly Ile Pro Pro Thr Glu Thr Glu
 645 650 655

Ala Tyr Phe Gly Ala Lys Glu Pro Glu Pro Ala Pro Pro Tyr His Ser
 660 665 670

Pro Glu Asp Ser Arg Glu His Val Asp Arg His Gly Cys Ile Val Lys
 675 680 685

Ile Val Arg Ser Ser Ser Ser Thr Gly Gln Lys Asn Phe Ser Ala Pro
 690 695 700

Pro Ala Ala Pro Pro Val Gln Cys Pro Pro Ser Thr Ser Trp Gln Pro
 705 710 715 720

Gln Ser His Pro Arg Gln Gly His Gly Thr Ser Pro Val Gly Asp His
 725 730 735

Gly Ser Leu Val Arg Ile Pro Pro Pro Pro Ala His Glu Arg Ser Leu
 740 745 750

Ser Ala Tyr Gly Gly Gly Asn Arg Ala Ser Met Glu Phe Leu Arg Gln
 755 760 765

Glu Asp Thr Pro Gly Cys Arg Pro Pro Glu Gly Asn Leu Arg Asp Ser
 770 775 780

Protein Complexes associated with APP-processing
 Asp Thr Ser Ile Ser Ile Pro Ser Val Asp His Glu Glu Leu Glu Arg
 785 790 795 800

Ser Phe Ser Gly Phe Ser Ile Ser Gln Ser Lys Glu Asn Leu Asp Ala
 805 810 815

Leu Asn Ser Cys Tyr Ala Ala Val Ala Pro Cys Ala Lys Val Arg Pro
 820 825 830

Tyr Ile Ala Glu Gly Glu Ser Asp Thr Asp Ser Asp Leu Cys Thr Pro
 835 840 845

Cys Gly Pro Pro Pro Arg Ser Ala Thr Gly Glu Gly Pro Phe Gly Asp
 850 855 860

Val Gly Trp Ala Gly Pro Arg Lys
 865 870

<210> 265

<211> 657

<212> PRT

<213> Homo sapiens

<400> 265

Met Arg Leu Lys Ile Gly Phe Ile Leu Arg Ser Leu Leu Val Val Gly
 1 5 10 15

Ser Phe Leu Gly Leu Val Val Leu Trp Ser Ser Leu Thr Pro Arg Pro
 20 25 30

Asp Asp Pro Ser Pro Leu Ser Arg Met Arg Glu Asp Arg Asp Val Asn
 35 40 45

Asp Pro Met Pro Asn Arg Gly Gly Asn Gly Leu Ala Pro Gly Glu Asp
 50 55 60

Arg Phe Lys Pro Val Val Pro Trp Pro His Val Glu Gly Val Glu Val
 65 70 75 80

Asp Leu Glu Ser Ile Arg Arg Ile Asn Lys Ala Lys Asn Glu Gln Glu
 85 90 95

His His Ala Gly Gly Asp Ser Gln Lys Asp Ile Met Gln Arg Gln Tyr
 100 105 110

Leu Thr Phe Lys Pro Gln Thr Phe Thr Tyr His Asp Pro Val Leu Arg
 115 120 125

Protein Complexes associated with APP-processing

Pro Gly Ile Leu Gly Asn Phe Glu Pro Lys Glu Pro Glu Pro Pro Gly
 130 135 140

Val Val Gly Gly Pro Gly Glu Lys Ala Lys Pro Leu Val Leu Gly Pro
 145 150 155 160

Glu Phe Lys Gln Ala Ile Gln Ala Ser Ile Lys Glu Phe Gly Phe Asn
 165 170 175

Met Val Ala Ser Asp Met Ile Ser Leu Asp Arg Asn Val Asn Asp Leu
 180 185 190

Arg Gln Glu Glu Cys Lys Tyr Trp His Tyr Asp Glu Asn Leu Leu Thr
 195 200 205

Ser Ser Val Val Ile Val Phe His Asn Glu Gly Trp Ser Thr Leu Met
 210 215 220

Arg Thr Val His Ser Val Ile Lys Arg Thr Pro Arg Lys Tyr Leu Ala
 225 230 235 240

Glu Ile Val Leu Ile Asp Asp Phe Ser Asn Lys Glu His Leu Lys Glu
 245 250 255

Lys Leu Asp Glu Tyr Ile Lys Leu Trp Asn Gly Leu Val Lys Val Phe
 260 265 270

Arg Asn Glu Arg Arg Glu Gly Leu Ile Gln Ala Arg Ser Ile Gly Ala
 275 280 285

Gln Lys Ala Lys Leu Gly Gln Val Leu Ile Tyr Leu Asp Ala His Cys
 290 295 300

Glu Val Ala Val Asn Trp Tyr Ala Pro Leu Val Ala Pro Ile Ser Lys
 305 310 315 320

Asp Arg Thr Ile Cys Thr Val Pro Leu Ile Asp Val Ile Asn Gly Asn
 325 330 335

Thr Tyr Glu Ile Ile Pro Gln Gly Gly Gly Asp Glu Asp Gly Tyr Ala
 340 345 350

Arg Gly Ala Trp Asp Trp Ser Met Leu Trp Lys Arg Val Pro Leu Thr
 355 360 365

Pro Gln Glu Lys Arg Leu Arg Lys Thr Lys Thr Glu Pro Tyr Arg Ser
 370 375 380

Pro Ala Met Ala Gly Gly Leu Cys Ala Ile Glu Arg Glu Phe Phe Phe
 385 390 395 400

Protein Complexes associated with APP-processing

Glu Leu Gly Leu Tyr Asp Pro Ser Leu Gln Ile Trp Gly Gly Glu Asn
405 410 415

Phe Glu Ile Ser Tyr Lys Ile Trp Gln Cys Gly Gly Lys Leu Leu Phe
420 425 430

Val Pro Cys Ser Arg Val Gly His Ile Tyr Arg Leu Glu Gly Trp Gln
435 440 445

Gly Asn Pro Pro Pro Ile Tyr Val Gly Ser Ser Pro Thr Leu Lys Asn
450 455 460

Tyr Val Arg Val Val Glu Val Trp Trp Asp Glu Tyr Lys Asp Tyr Phe
465 470 475 480

Tyr Ala Ser Arg Pro Glu Ser Gln Ala Leu Pro Tyr Gly Asp Ile Ser
485 490 495

Glu Leu Lys Lys Phe Arg Glu Asp His Asn Cys Gln Ser Phe Lys Trp
500 505 510

Phe Met Glu Glu Ile Ala Tyr Asp Ile Thr Ser His Tyr Pro Leu Pro
515 520 525

Pro Lys Asn Val Asp Trp Gly Glu Ile Arg Gly Phe Glu Thr Ala Tyr
530 535 540

Cys Ile Asp Ser Met Gly Lys Thr Asn Gly Gly Phe Val Glu Leu Gly
545 550 555 560

Pro Cys His Arg Met Gly Gly Asn Gln Leu Phe Arg Ile Asn Glu Ala
565 570 575

Asn Gln Leu Met Gln Tyr Asp Gln Cys Leu Thr Lys Gly Ala Asp Gly
580 585 590

Ser Lys Val Met Ile Thr His Cys Asn Leu Asn Glu Phe Lys Glu Trp
595 600 605

Gln Tyr Phe Lys Asn Leu His Arg Phe Thr His Ile Pro Ser Gly Lys
610 615 620

Cys Leu Asp Arg Ser Glu Val Leu His Gln Val Phe Ile Ser Asn Cys
625 630 635 640

Asp Ser Ser Lys Thr Thr Gln Lys Trp Glu Met Asn Asn Ile His Ser
645 650 655

Val

Protein Complexes associated with APP-processing

<210> 266

<211> 501

<212> PRT

<213> Homo sapiens

<400> 266

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
 1 5 10 15

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205

Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220

Protein Complexes associated with APP-processing

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285

Asn Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300

Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380

Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415

Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430

Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445

Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460

Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
 465 470 475 480

Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
 485 490 495

Protein Complexes associated with APP-processing
Ile Ser Leu Leu Lys
500

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/13980

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/47 C07K16/18 G01N33/68 A61K38/17 C12N15/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K G01N A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE SFN ABSTRACTS 2003 [Online] 33rd annual meeting of the society for neurosc 10 November 2003 (2003-11-10), HOPF, C. ET AL.: "Discovery of new therapeutic targets by integrated protein pathway and chemical proteomic analysis of APP processing." XP002292236 retrieved from HTTP://SFN.SCHOLARONE.COM/ITIN2003/MAIN.HT ML Database accession no. ABSTRACT 406.5 the whole document	1-12, 17-45
Y	WO 01/67097 A (BLACKSTOCK WALTER ; GLAXO GROUP LTD (GB); ROWLEY ADELE (GB); HALE RICH) 13 September 2001 (2001-09-13) the whole document ----- -/--	1-12, 17-45



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 August 2004

Date of mailing of the international search report

12.11.2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Smalt, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/13980

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/09716 A (EUROP LAB MOLEKULARBIOLOG ; SERAPHIN BERTRAND (DE); RIGAUT GUILLAUME () 24 February 2000 (2000-02-24) cited in the application the whole document -----	
A	US 6 130 317 A (REED JOHN C ET AL) 10 October 2000 (2000-10-10) * see the whole document, in particular column 27, first full paragraph * the whole document -----	
A	US 6 383 758 B1 (FRASER PAUL E ET AL) 7 May 2002 (2002-05-07) column 13, line 64 - column 14, paragraph 1 -----	
A	WO 02/33114 A (MYRIAD GENETICS INC) 25 April 2002 (2002-04-25) the whole document -----	
A	MARAMBAUD P ET AL: "Presenilin1 forms Ca++-dependent complexes with the E-cadherin/catenin cell adhesion system" SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 25, no. 1-2, 1999, page 1299, XP001194698 & 29TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE.; MIAMI BEACH, FLORIDA, USA; OCTOBER 23-28, 1999 ISSN: 0190-5295 the whole document -----	
A	SHIOI J ET AL: "Presenilin1 forms a 600 kDa molecular complex with components of adheren junctions" SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 25, no. 1-2, 1999, page 1601, XP001194697 & 29TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE.; MIAMI BEACH, FLORIDA, USA; OCTOBER 23-28, 1999 ISSN: 0190-5295 the whole document -----	
A	GEORGAKOPOULOS A ET AL: "Presenilin-1 forms complexes with the cadherin/catenin cell-cell adhesion system and is recruited to intercellular and synaptic contacts." MOLECULAR CELL. DEC 1999, vol. 4, no. 6, December 1999 (1999-12), pages 893-902, XP002292239 ISSN: 1097-2765 cited in the application the whole document -----	
	-/--	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/13980

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1- 12, 17 - 42 all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 35-40, to the extent that they pertain to in vivo use, are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 42-44 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Present claims 1-12 and 17-45 relate to an extremely large number of possible protein complexes. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the complexes claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the complexes comprising ALL of the individual proteins listed under each complex in table 1 in column 3.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-12,17-42, all partially

Presenilin-1 complex according to table 1, methods for its production, recombinant expression, antibodies thereto which do not bind to the individual proteins, method for identifying binding agents and/or modulators, and diagnostic and pharmaceutical uses thereof.

Inventions 2-14: claims 1-12 and 17-42, all partially

Subject-matter essentially as defined for invention 1 above, but limited to the respective protein complexes as listed in table 3 and detailed in table 1 of the application.

For the sake of conciseness, the first invention has been defined in detail, the subject-matter of inventions 2-14 has been defined by analogy thereto.

Invention 15: claims 12-16,18-21 and 23-25, all partially

CGI-147 protein, nucleic acid encoding it, host cell, kit, array, pharmaceutical composition, and method for screening for binding molecule.

Inventions 16-102: claims 12-16,18-21 and 23-25, all partially

Subject-matter essentially as defined for invention 15 above, but limited to the individual proteins listed in column 6 of table 1 of the application.

For the sake of conciseness, the first invention has been defined in detail, the subject-matter of inventions 2-14 has been defined by analogy thereto.

Invention 103: claim 45, partially

Proteins listed in column 5 of table 1 as a target for an active agent of a pharmaceutical.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/13980

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0167097	A	13-09-2001	AU 4079301 A EP 1259822 A2 WO 0167097 A2	17-09-2001 27-11-2002 13-09-2001
WO 0009716	A	24-02-2000	AT 223491 T AU 762961 B2 AU 5736299 A CA 2340974 A1 DE 69902796 D1 DE 69902796 T2 DE 1105508 T1 DK 1105508 T3 WO 0009716 A1 EP 1231276 A1 EP 1105508 A1 ES 2183601 T3 JP 2002522085 T PT 1105508 T US 2002061513 A1	15-09-2002 10-07-2003 06-03-2000 24-02-2000 10-10-2002 07-08-2003 21-02-2002 06-01-2003 24-02-2000 14-08-2002 13-06-2001 16-03-2003 23-07-2002 31-01-2003 23-05-2002
US 6130317	A	10-10-2000	US 5837838 A US 6545128 B1 AU 6760798 A WO 9840397 A1	17-11-1998 08-04-2003 29-09-1998 17-09-1998
US 6383758	B1	07-05-2002	US 2002127541 A1 AU 1957299 A WO 9935501 A1	12-09-2002 26-07-1999 15-07-1999
WO 0233114	A	25-04-2002	AU 1323902 A AU 1324102 A AU 1458902 A AU 1459002 A WO 0232286 A2 WO 0233112 A2 WO 0233113 A2 WO 0233114 A2 US 2003186317 A1 US 2002119155 A1 US 2002119927 A1 US 2002115119 A1 US 2002106773 A1 US 2002114799 A1 US 2002164655 A1 US 2002106676 A1 US 2002115606 A1 US 2002124273 A1 US 2002115607 A1	29-04-2002 29-04-2002 29-04-2002 29-04-2002 25-04-2002 25-04-2002 25-04-2002 25-04-2002 02-10-2003 29-08-2002 29-08-2002 22-08-2002 08-08-2002 22-08-2002 07-11-2002 08-08-2002 22-08-2002 05-09-2002 22-08-2002
WO 2004007544	A	22-01-2004	WO 2004007544 A2	22-01-2004

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